Archives of Dermatology and Syphilology

VOLUME 48 AUGUST 1943 NUMBER 2

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KERATOSIS FOLLICULARIS

A STUDY OF FOUR CASES

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In 1938 Peck [1] studied a case of Darier's disease in a man aged 25. It occurred to him that since the chief pathologic change is a follicular dyskeratosis, the disease might possibly be due to vitamin A deficiency. He therefore tried the effect of large doses of this vitamin and obtained considerable clinical improvement.

Before giving an account of the cases which have since been reported or those to be here described, it is well to consider first the cutaneous signs which characterize a vitamin A deficiency and second the tests by which this deficiency state can be assessed. The symptoms of avitaminosis A are of two main types, night blindness and a generalized epithelial metaplasia affecting the basal cells and resulting in hyperkeratosis. In the eye the terminal state is known as xerophthalmia or keratomalacia. In the skin the changes are most noticeable around the follicular orifices, and the resultant state has been called phrynoderma or toadskin. Of the physiologic mechanism at the root of these epidermal changes nothing is known. An obstacle to investigation is the absence, at least in measurable quantity, of vitamin A in the epidermal cells as proved by chemical assay [2] and fluorescence tests.[3]

CUTANEOUS SIGNS OF AVITAMINOSIS A

Advanced states of vitamin A deficiency, such as phrynoderma and keratomalacia, have been observed chiefly in Africa and the Orient and are rare in Great Britain and the United States. Early stages of this avitaminosis A are, however, not uncommon. For instance, the characteristic lesion of phrynoderma observed by Frazier and Hu [4] among Chinese soldiers has since been found by Youmans and Corlette [5] and by Lehman and Rapaport [6] among white persons in the United States and has been noted in a mild form by Pemberton [7] in 5 per cent of a group of 3,000 children in Great Britain. Lehman and Rapaport considered that keratosis follicu-

1. Peck, S. M.; Chargin, L., and Sobotka, H.: Keratosis Follicularis (Darier's Disease), Arch. Dermat. & Syph. **43**:223 (Feb.) 1941.
2. Popper, H.: Vitamin A: The Distribution of Vitamin A in the Body, J. Mt. Sinai Hosp. **7**:119 (Sept.) 1940.
3. Cornbleet, T., and Popper, H.: Properties of Human Skin Revealed by Fluorescence Microscopy, Arch. Dermat. & Syph. **46**:59 (July) 1942.
4. Frazier, C. H., and Hu, C. K.: Cutaneous Lesions Associated with a Deficiency in Vitamin A in Man, Arch. Int. Med. **45**:507 (Sept.) 1931.
5. Youmans, J. B., and Corlette, M. B.: Specific Dermatoses Due to Vitamin A Deficiency, Am. J. M. Sc. **195**:644 (May) 1938.
6. Lehman, E., and Rapaport, H. G.: Cutaneous Manifestations of Vitamin A Deficiency in Children, J. A. M. A. **114**:386 (Feb. 3) 1940.
7. Pemberton, J.: Follicular Hyperkeratosis: A Sign of Malnutrition? Lancet **1**:871 (May 11) 1940.

laris, lichen spinulosus and ichthyosis follicularis are all descriptive terms for the cutaneous symptoms of "pure" vitamin A deficiency which they observed in New York city. The following conditions have been suggested by various investigators as associated with a deficiency of vitamin A alone, or with multiple avitaminoses, and beneficial results in response to therapy have been claimed by many:

1. Follicular hyperkeratosis with local loss of hair.[8]
2. Xeroderma, including some forms of ichthyosis, possibly due to keratinization affecting the sebaceous and sweat glands.[9]
3. Pigmentation due to melanoblasts in the basal layer of the epidermis. After involution of the lesions due to vitamin A deficiency, a depressed scar with a zone of pigment is often left.[10]
4. Dystrophy of the nails, with striation, stippling, white spots and fragility.[11] This resembles other dystrophies and is not specific.
5. An acneform eruption of the face, occurring most frequently in adolescents.[12]
6. Glazed, red or beefy tongue, with aphthae, swollen gums and low resistance to monilial infection.[13]
7. Similar changes in the vulva or vagina.[14]
8. Perlèche, or maceration and fissuring of the labial commissures.[15]
9. Alopecia as seen in folliculitis decalvans and possibly also the alopecia of thyrotoxicosis and pregnancy.[10a]
10. Lowered tolerance of the skin to bacterial infection and to irritant contact.[16]
11. Seborrheic dermatitis and contact dermatitis.[17]

None of these symptoms is, of course, specific, and the evidence assigning some of them to vitamin A deficiency is decidedly inadequate. Others are now considered to be symptoms of deficiency of other vitamins. Thus the "tomato" red tongue with atrophy of the papillae is characteristic of nicotinic acid deficiency, and the congested "beefsteak" purple tongue, of ariboflavinosis. Angular stomatitis and cheilosis are also symptoms of deficiency of riboflavin. Loewenthal,[8] who examined 450 cases of apparently pure vitamin A deficiency in Uganda, concluded that " 'sore mouth,' 'itchy scrotum,' perlèche, changes in the hair and increased susceptibility to general infection are not sequelae of vitamin A deficiency in man." It is now recognized that pure deficiencies of single dietary factors rarely occur in

8. Loewenthal, L. J. A.: The Manifestations of Vitamin A Deficiency in Man, Ann. Trop. Med. **29**:407 (Dec.) 1935. Frazier and Hu.[4]

9. Baer, H. L., and Vogel, H. R.: The Biophotometric Study of Vitamin A in Dermatological Conditions, Urol. & Cutan. Rev. **44**:176 (March) 1940. Frazier and Hu.[4]

10. (*a*) Keil, H.: The Follicular Lesions of Vitamin A and C Deficiencies, Am. J. Digest. Dis. **5**:40 (March) 1938. (*b*) Goodman, H.: Dermatologic Symptoms of Vitamin Deficiencies, Arch. Dermat. & Syph. **38**:389 (Sept.) 1938. Frazier and Hu.[4]

11. Schwemmler, B.: Einfluss von Vitamin A in Haar- und Nagelwachstum, München. med. Wchnschr. **86**:1226 (Aug. 11) 1939. Keil.[10a]

12. Loewenthal.[8] Baer and Vogel.[9] Keil.[10a]

13. Mouriquand, B., and Gaté, G.: Avitaminoses en dermatologie, Ann. de dermat. et syph. **6**:881 (Oct.) 1935.

14. Unna, K., in discussion on papers by Gross, P.: Nicotinic Acid Deficiency Secondary to Removal of a Portion of the Gastrointestinal Tract, and Pityriasis Rubra Pilaris and Vitamin Therapy, Arch. Dermat. & Syph. **44**:270 (Aug.) 1941.

15. Nicholas, L.: A Study of Vitamin A Deficiency in Ceylon with Special Reference to the Statistical Incidence of Phrynoderma or "Sore Mouth," Indian M. Gaz. **69**:241 (May) 1934.

16. (*a*) Dainow, L.: Treatment of Occupational Dermatitis with Vitamins A and D, cited by Wise, F., and Sulzberger, M.: The 1939 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1940, p. 452. (*b*) von Kibéd, A. V.: Newer Contributions to Treatment on Seborrhoeic Disorders Due to Gastro-Intestinal Disturbances (Vitamin Deficiencies), cited by Wise, F., and Sulzberger, M.: The 1940 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1941, p. 480. Baer and Vogel.[9]

17. Mackay, H.: Vitamin A Deficiency in Children, Arch. Dis. Childhood **9**:65 (April); 133 (June) 1934. Baer and Vogel.[9] von Kibéd.[16b]

clinical medicine. This accounts in part for the confusing variety of nonspecific symptoms which have been claimed by various authors to improve after vitamin therapy.

A perusal of the foregoing list of symptoms makes it clear that there is no decided resemblance between the picture seen in accepted cases of avitaminosis A and that observed in Darier's disease. Nor is the existence of dyskeratosis a reliable link between the two, since dyskeratosis with the production of "grains" and "corps ronds" is seen in a number of dermatoses, such as molluscum contagiosum, Paget's disease, Bowen's disease and certain types of papilloma and epithelioma, in which one would not suspect a vitamin deficiency of playing any etiologic role. There are some suggestive links between Darier's disease and avitaminosis A, but they are so tenuous as to be scarcely worth mentioning. The disease, for instance, is not uncommonly associated with endocrine disturbance, and some obscure interrelation between the endocrine glands and vitamin metabolism has been suggested by numerous writers.[18] Darier's disease is genetically inherited, and endocrine imbalance is frequently noted in familial diseases. It has been pointed out too [1] that in its symmetric distribution and in the sites affected Darier's disease resembles seborrheic dermatitis, and von Kibéd [6b] has suggested that with some forms of this disease there is a primarily faulty gastric secretion, which results in abnormal digestion and absorption, especially of the fat-soluble vitamins A and D. It is true that in some cases seborrheic dermatitis does respond to treatment with halibut liver oil, but a clear case for avitaminosis has certainly not been established.

If vitamin imbalance is at the root of Darier's disease, Sulzberger and Wise suggested [19] that one should use the term "dysvitaminosis" rather than avitaminosis or hypovitaminosis, because the fault is likely to be not so much a simple reduction or absence of the vitamin as some more complicated error in its utilization. Some tissues of the body are affected, while other tissues, or other parts of the same tissue, show no abnormality.

TESTS FOR ASSESSING AVITAMINOSIS A

1. *Dark adaptation.*—In contrast with investigations of the epidermis, dark adaptation tests have proved one of the most useful means of detecting states of human vitamin A deficiency. The physiologic basis of this method is the part played by vitamin A in the photochemical cycle of visual purple or rhodopsin in the retina. This is at present the only one of its physiologic functions of which we have any precise knowledge. The retina of many vertebrates, including man, possesses two types of photoreceptor cells, the cones, which are most numerous at the fovea and function in daylight or color vision, and the rods, which predominate in the parafovea and are active in twilight or nocturnal vision. Visual purple is the photosensitive pigment of the rods. It is a complex chromoprotein which is broken down by light in at least two stages, liberating vitamin A. Although the behavior of visual purple within the rods is not yet fully understood, this cycle does express concisely the knowledge of the role of vitamin A in the system. The energy released

18. (*a*) Sutton, T. S., and Brief, B. J.: Cellular Changes in the Anterior Hypophyses of Vitamin A Deficient Rats, Endocrinology **23**:211 (Aug.) 1938. (*b*) Clausen, S. W., and McCoord, A. B.: The Carotinoids and Vitamin A of the Blood, J. Pediat. **13**:635 (Nov.) 1938. (*c*) Sulzberger, M., in discussion on papers by Gross, P.: Nicotinic Acid Deficiency Secondary to Removal of a Portion of the Gastrointestinal Tract, and Pityriasis Rubra Pilaris and Vitamin Therapy, Arch. Dermat. & Syph. **44**:270 (Aug.) 1941. Unna.[14]

19. Wise, F., and Sulzberger, M.: The 1941 Year Book of Dermatology and Syphilology, Chicago, the Year Book Publishers, Inc., 1942, p. 449.

by the breakdown of visual purple in the rods is believed to initiate the nervous impulses which carry the sensation of light to the central nervous system. In darkness visual purple is resynthesized and free vitamin A disappears from the retina. At the same time the sensitivity of the eye increases roughly in proportion to the concentration of visual purple. The process, which is known as dark adaptation, continues until the rods contain their maximum concentration. For practical purposes, it is virtually complete after thirty to forty minutes in darkness. The amount of available vitamin A, therefore, limits the concentration of visual purple which the rods are able to synthesize. In experimental human vitamin A deficiency dark adaptation is impaired, and when the deficiency is corrected the sensitivity of the eyes in night vision returns to normal.[20]

This precise knowledge of the role of vitamin A in night vision has been used to assess vitamin A nutrition. The rise of visual threshold, known as night blindness, can be measured accurately and is usually the first demonstrable symptom of deficiency of vitamin A in man. It increases progressively as the avitaminosis develops. The experiments in human deficiency aforementioned form an exact basis for the design of a routine clinical procedure, and one investigation of a population by this means has already been described.[21]

In the cases which will shortly be considered, dark adaptation was measured with the portable adaptometer of Wald. This instrument and the method of testing have been described in full elsewhere.[22] Measurements were made of the visual threshold of a retinal field of 2.5 degrees visual angle, fixated 6.0 degrees below the fovea, with flashes of one-fiftieth second duration to the full radiation of a tungsten filament lamp. Readings normally were binocular. Values of visual threshold were expressed as the logarithm of micromillilamberts (i. e., log millilamberts $\times 10^{-6}$). The advantages of these units for recording the data have been discussed in full elsewhere.[23]

The following procedure was adopted for routine clinical tests. Subjects were kept in darkness for about twenty minutes without previous light adaptation, and a series of readings of the visual threshold was then made until stable values were obtained. The actual time spent in darkness is immaterial, since this method is designed to measure only the final stable level of sensitivity attained by the rods. This value is the most sensitive single index of vitamin A deficiency.

The criterion of deficiency is all-important. It is commonly thought that a single demonstration of an abnormally high visual threshold is sufficient evidence for diagnosing a state of vitamin A deficiency. Actually it is decidedly inadequate, since various other conditions also cause night blindness (e. g., retinitis pigmentosa, hepatic disease, hereditary absence of rod function and changes in the ocular media associated with senility). It is essential, therefore, to show that a poor visual

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20. (*a*) Wald, G., and Steven, D.: An Experiment in Human Vitamin A Deficiency, Proc. Nat. Acad. Sc. **25**:344 (July) 1939. (*b*) Booher, L. E.; Callison, E. C., and Hewston, E. M.: An Experimental Determination of the Minimum Vitamin A Requirements of Normal Adults, J. Nutrition **17**:317 (April) 1939. (*c*) Hecht, S., and Mandelbaum, J.: Vitamin A and Dark Adaptation, J. A. M. A. **112**:1910 (May 13) 1939; (*d*) Dark Adaptation and Experimental Human Vitamin A Deficiency, Am. J. Physiol. **130**:651 (Oct.) 1940. (*e*) Wagner, K. H.: Die experimentelle Avitaminose beim Menschen, Ztschr. f. physiol. Chem. **264**:153, 1940.

21. Steven, D., and Wald, G.: Vitamin A Deficiency: A Field Study in Newfoundland and Labrador, J. Nutrition **21**:461 (May) 1941.

22. Wald, G.: A Portable Visual Adaptometer, J. Optic. Soc. America **31**:235 (March) 1941. Dow, D., and Steven, D.: An Investigation of Simple Methods for Diagnosing Vitamin A Deficiency by Measurements of Dark Adaptation, J. Physiol. **100**:256 (Nov.) 1941.

23. Wald, G.; Jeghers, H., and Arminio, J.: An Experiment in Human Diets on Night Blindness, Am. J. Physiol. **123**:732 (Sept.) 1938. Hecht and Mandelbaum.[20c]

threshold is in fact due to deficiency of vitamin A. The criterion defined by Steven and Wald [21] was the vitamin A–labile threshold. A person was regarded as deficient only when the threshold, whatever its initial value, was lowered significantly by administration of vitamin A. A threshold which could not be improved was said to be vitamin A–stable.

It is of course important to determine the smallest amount of improvement which can be considered significant. It must be greater than the day to day range of variation of visual threshold in normal persons. This is about 0.3 log unit (i. e., a factor of approximately two times .27.29). An improvement of the visual threshold greater than 0.3 log unit following vitamin A therapy is therefore unlikely to be due to chance fluctuations of sensitivity, such as occur from day to day in normal persons. The uncertainty with which a vitamin A–labile threshold can be diagnosed is increased if more than one preliminary test is made before therapy is begun and if any improvement noticed can be confirmed by further tests. "Learning" effects are virtually absent from this type of dark adaptation test.

2. *Level of vitamin A and carotene in blood.*—Measurements of the content of vitamin A in the blood, although in wide use, do not provide a reliable criterion of mild states of deficiency. The unreliability is due to three main reasons:

A. Most of the methods used at present are far from satisfactory. Morton [24] has discussed the technical problems in the estimation of vitamin A in various mediums in which other carotenoids with similar spectrographic and chemical characteristics—are also present in variable proportions. The generally accepted unit of vitamin A, the international unit (and its equivalent, the U. S. P. unit), expresses the biologic activity of a substance, and it is still uncertain whether measurements of a chemical or physical property, such as the Carr-Price reaction or spectrographic analysis in organic mediums, bear a constant relation to the biologic unit.

B. There is no single critical level of vitamin A below which persons in general can be said to be deficient. There does appear to be a critical level below which progressive impairment of dark adaptation becomes apparent, but this is an individual characteristic and varies widely in different persons.[25]

C. Clausen and McCoord [18b] have shown that variations between single determinations of vitamin A concentration in plasma are great even in normal persons.

A low value for vitamin A in the blood, therefore, is not in itself evidence of deficiency, although when it is associated with poor dark adaptation a probable deficiency state is indicated. The simple demonstration that a visual threshold is vitamin A–labile, however, is unequivocal evidence that the subject is deficient. For this reason, few tests of the vitamin A content of the blood have been made in the following cases. Difficulties of transportation under wartime conditions also limited the possibilities of investigation.

REPORT OF CASES

CASE 1.—M. H., a woman aged 49, first noticed a thick, scaly eruption on the scalp and behind the ears when she was 23. She saw various doctors and went to two dermatologic clinics in London, but the disease remained unaltered despite local treatment. In the spring of 1941 it became worse and was complicated for a time with secondary infection and lymphadenitis. In September a more careful examination showed that beneath the crusts there were hyperkeratotic follicles and that some of these, especially behind the ears, had central

24. Morton, R. A.: Fat-Soluble Vitamins, in Luck, J. M., and Smith, J. H. C.: Annual Review of Biochemistry, Stanford University, Calif., Annual Reviews, Inc., 1942, vol. 11, p. 365.

25. Yudkin, S.: Vitamin A and Dark Adaptation: Effect of Alcohol, Benzedrene and Vitamin C, Lancet **2**:787 (Dec. 27) 1941. Steven, D.: Tr. Ophth. Soc. U. Kingdom, 1942, to be published.

horny plugs. Two barely perceptible symmetric patches at the base of the neck on either side suggested the diagnosis of keratosis follicularis (Darier). On inquiry it was found that the patient's son (case 2) had a similar disease.

A biopsy was performed, and the following report was received from Dr. A. H. Robb Smith: "The section shows all the characteristic features of Darier's disease. There is generalized thickening of the epidermis, with flattening of the rete pegs and melanosis of the malpighian layer. This is associated with foci of chronic inflammatory cells (chiefly lymphocytes) in the corium, particularly near the blood vessels. The specific focal lesion is characterized by a great degree of hyperkeratosis and parakeratosis, with edema and degeneration of the squamous cells of the epithelium and the formation of two sorts of products, the 'corps ronds' and the 'grains.'"

A dark adaptation test was then made. The final rod threshold value was good (1.975 log micromillilamberts). She was then given halibut liver oil containing 18,000 international units of vitamin A [26] daily. Two weeks later she reported improvement, and after three weeks her neck and ears had cleared almost completely and the crusting on the scalp was diminished. A second dark adaptation test after she had been receiving vitamin A for a month revealed a value almost identical with the first (1.9 log micromillilamberts). After three months' treatment with vitamin A, the scalp was healthy, except for a circular area about 4 inches (10 cm.) in circumference, which was hyperkeratotic but only slightly crusted. Nine months later this too had gone. She then ceased for two months to take vitamin A. At the end of this period her blood was tested and gave the following results: carotene, 53 international units per hundred cubic centimeters of plasma (rather low); vitamin A, 96 international units per hundred cubic centimeters of plasma (normal). The woman was a hotel manager, and she and her son (case 2) lived on a good mixed diet.

CASE 2.—E. H., a youth aged 18, son of M. H. (case 1), had a symmetric eruption involving the crown of the head, the base of the neck on either side and a lozenge-shaped area in the interscapular region. The eruption consisted of firm, elevated papules, averaging 0.5 cm. in diameter, with central hyperkeratotic plugs. The papules were red or skin colored, and many were covered with thick, brownish crusts. The disease first became apparent after the patient had an attack of measles at the age of 12. The patch on the back appeared a little later and was attributed to sunburn. During six years the areas spread slightly. The patient never had treatment. He was not concerned about his dermatosis until he was refused by the R. A. F. on account of it.

A dark adaptation test was made, and the final rod threshold was found to be good (1.95 log micromillilamberts). He was then given halibut liver oil containing about 27,000 international units daily. A second test about a month later revealed a small but not significant improvement in dark adaptation (1.775 log micromillilamberts). After three months there was slight improvement, but hardly more than might have been achieved with local treatment. Nine months later the condition was the same. He stopped treatment for two months with no clinical change, and his blood was then tested. It showed: carotene, 43 international units per hundred cubic centimeters of plasma; vitamin A, 83 international units per hundred cubic centimeters of plasma. The test was repeated a month later, and before he had taken any more vitamin A, with the following results: carotene, 250 international units per hundred cubic centimeters of plasma; vitamin A, 90 international units per hundred cubic centimeters of plasma. Thus, while the vitamin A level remained fairly constant and normal, the carotene level was on one occasion rather low and on the other very high. But on the occasion when his carotene level was low, his dark adaptation was normal (1.775 log micromillilamberts, just as it had been earlier). This bears out the thesis that a low carotene level is in itself no proof of vitamin A deficiency.

CASE 3.—F. G. was a farm hand aged 35. In 1937, after some acute infection of unknown nature which involved the scalp, face, neck and arms, patches of scaling and roughness developed in these regions. When first seen, in November 1940, he had symmetric, dark brown, grouped, dyskeratotic papules on the scalp, forehead, sides of the neck and extensor aspects of the forearms. After treatment with tar for eight months the lesions showed only slight improvement, and there was no diminution of the area involved.

A biopsy report from Dr. Robb Smith stated: "The sections showed generalized hyperkeratosis, associated with broadening of the epidermis, and in some places parakeratosis. Two

26. All 4 patients were given vitamin A therapy in the form of halibut liver oil capsules (Crookes). This preparation also contains vitamin D in the proportion of 100 U. S. P. units of vitamin A to 511 U. S. P. units of vitamin D. The latter vitamin does not affect dark adaptation or other visual processes.

areas of the epidermis exhibit the interstitial edema with degeneration of the squamous but not of the basal layer which is characteristic of Darier's disease. 'Corps ronds' can be seen. In the corium, there is lymphocytic and histiocytic infiltration."

Dark adaptation was tested in July 1941 and found to be good (rod threshold 1.9 log micromillilamberts). His vitamin A and carotene intake were good, green vegetables were eaten daily, the full fat ration of 2 ounces (56.6 Gm.) of butter and 4 ounces (113.4 Gm.) of margarine with ½ pound (226.8 Gm.) of cheese each week, and rather less than ½ pint (0.25 liter) of milk daily. He was then given halibut liver oil containing 27,000 international units of vitamin A daily. Two months later he wrote to say that he was improving and that his arms were "something lovely," but he was unable to visit the hospital again until February 1942. His scalp and face were then entirely clear. Low down on the neck there were still a number of papules, but the area had diminished in size, and the papules themselves were much smaller. The patch which had previously covered more than half the back of his forearm had shrunk to a circle about 1 inch (2.5 cm.) in diameter. The skin over the cleared areas was slightly pigmented. He had not taken halibut liver oil for the past three months and stated that the improvement had occurred while he was taking it and that when he stopped his condition remained stationary. He was satisfied with the result and came to the hospital only by request. After several months without vitamin therapy he had a slight return of cutaneous lesions and reappeared for treatment. He was tested again with the following results: darp adaptation, rod threshold, 1.94 log micromillilamberts; carotene, 220 U. S. P. units per hundred cubic centimeters of plasma; vitamin A, 47 international units per hundred cubic centimeters of plasma. After a month of daily treatment with 27,000 international units of vitamin A he wrote that he was again better but could not spare time to come to the hospital.

CASE 4.—M. G., a woman aged 34, a sister of F. G. (case 3), first noticed the eruption in her early twenties. It affected the middle of the back, the sacral area, the loins and the inguinal regions. There was also coloboma iridis in the right eye. She first appeared for treatment in June 1942, when she was eight months pregnant.

Dark adaptation gave a normal rod threshold (1.97 log micromillilamberts). Biopsy confirmed the diagnosis. She was given halibut liver oil containing 27,000 international units daily. After the birth of her baby the dyskeratosis spread to her thighs and presternal region. After four months of treatment the eruption was unaltered. She then ceased attendance and abandoned vitamin treatment. Her diet was reasonably good. Three months later she was reexamined, with the following results: dark adaptation, 1.88 log micromillilamberts, i. e., approximately unchanged; carotene, 145 international units per hundred cubic centimeters of plasma; vitamin A, 78 international units per hundred cubic centimeters of plasma. In short, there was no evidence, clinical or otherwise, of vitamin deficiency.

COMMENT

Though dermatologists at clinical meetings (see the transactions regularly published in the ARCHIVES) have often mentioned both favorable and unfavorable effects of the administration of vitamin A or of vitamins A and D in cases of Darier's disease, the only report which includes clinical tests is the account of 4 cases by Peck, Chargin and Sobotka.[1] In all of these cases the carotene content of the blood was within normal limits, but the vitamin A level, despite a normal diet, was lowered, though not greatly (47 to 48 international units per hundred cubic centimeters of serum). In 1 case dark adaptation tested by the Hecht method was normal, in 2 it was apparently not tested and in the fourth it was "one-tenth normal." The clinical course in 1 case was not recorded. In the other 3, after massive vitamin therapy (200,000 international units of vitamin A daily) the affected patches cleared considerably but did not entirely disappear. The level of vitamin A in the blood rose slowly in 1 case, suggesting poor absorption from the gastrointestinal tract. In another, a rapid drop from the high level in the blood occurred as soon as the large oral doses were discontinued. Peck suggested that the disease is a "physiologic nevus," with a hereditary defect in absorption of vitamin A or in conversion of provitamin A (carotene) manifesting itself in the skin as dyskeratosis.

The 4 patients herein considered included a mother and her son and a brother and his sister. No other member of either family was known to have the dis-

ease, and the parents were not consanguineous. In 2 patients the disease first appeared after a previous ailment, measles in the first and another (unknown) dermatosis in the second. The results of repeated dark adaptation tests were always normal. Vitamin A was normal in 3 patients and fairly low in 1 (47 international units per hundred cubic centimeters of plasma). Carotene levels were irregular, being high in 1, low in 2 and first low and then high a month later in the fourth. These findings are probably variations of no significance, as considerable variation is known to exist in normal persons. Response was lacking in 2 patients, and in 2 it was complete. In both of the latter the disease had lasted unchanged for years, and 1 had had intensive local treatment without result. The response was slowly established. In 1 of the patients a slight recurrence followed the cessation of vitamin therapy for some months, and its resumption again brought about improvement.

According to Ford,[27] Darier's disease results from two different types or genetic disturbance. In some families it is inherited as a sex-linked dominant, and in others (see also Hitch, Callaway and Moseley [28]) it is not sex linked and occurs as an autosomal dominant. It was tempting to suppose that one genetic type might account for the responsiveness to vitamin A and the other genetic type for the refractoriness, but this supposition is ruled out by the behavior of the 4 patients discussed in this report, since in 1 member of each family the disease was refractory and in the other it was responsive.

One can hardly postulate a simple avitaminosis on the basis of these observations. But it is difficult, on the other hand, to dismiss the vitamin factor entirely, when so decided a clinical response is seen in a disease which had previously remained unchanged for years.

SUMMARY

A brief account is given of the cutaneous signs ascribed to avitaminosis A.

The tests for assessing deficiency are discussed, and it is suggested that the dark adaptation test when properly applied is the best, whereas the levels of vitamin A and carotene in the blood are of uncertain significance.

Four cases of Darier's disease in patients belonging to two different families are recorded. Tests revealed no evidence of vitamin deficiency. In 1 member of each family, there was complete involution with vitamin A therapy; the other member was unaffected.

This result rules out the possibility that the two known genetic types of Darier's disease might correspond to two different reactions, positive and negative, to vitamin A therapy.

45 Banbury Road.

27. Ford, E. B.: Genetics for Medical Students, London, Methuen & Co., Ltd., 1942.

28. Hitch, J. M.; Callaway, J. L., and Moseley, V.: Familial Darier's Disease (Keratosis Follicularis), South. M. J. **34**:578 (June) 1941.

BENEFICIAL EFFECT OF SMALLPOX VACCINE ON RECURRENT APHTHOUS ULCERS OF MOUTH AND TONGUE

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The current methods of treatment of recurrent aphthous ulcers are of little value. I was induced to employ repeated inoculations with smallpox vaccine in 2 cases of aphthous ulcer on the assumption that the condition is probably caused by a virus akin to that of herpes simplex, a disease which, when recurrent, is frequently controlled by such treatment. In both the following cases the disease had been unaffected by local applications of caustic materials or by the use of diets or vitamins.

REPORT OF CASES

CASE 1.—V. C., a white man aged 43, was first seen on April 16, 1941. He gave a history of having had "canker sores" in the mouth practically continuously for the preceding two and one-half years. Physical examination showed no abnormalities except for the oral lesions, which consisted of large aphthous ulcers on the inner surface of the lower lip and the left side of the tongue and of two similar, smaller lesions on the right side of the tongue. At the end of one week the lesions were practically healed, and two new ones were developing on the tongue. Two weeks later there was a large ulcer on the inner surface of the lower lip. The patient was not seen again until September 30, when the tongue and both cheeks presented numerous aphthae. Inoculation with smallpox vaccine was commenced on October 14, at which time there was a large ulcer on the inner surface of the lower lip, and was repeated for a total of twelve doses at intervals of two weeks, except between the second and the third and the ninth and the tenth dose, when the intervals were four and seven weeks respectively. At the time of the second inoculation there was a new, large ulcer on the inner aspect of the lower lip. Fresh lesions continued to appear during the succeeding four weeks. None, however, developed from November 25 to Jan. 7, 1942, when a small ulcer appeared on the inner aspect of the lower lip. On February 9 a fresh sore arose on the tongue, and at the time of the tenth inoculation, on April 7, there were as many ulcers in the mouth as there had been at any time. At the conclusion of the twelfth inoculation, on May 5, the patient stated the belief that, while the treatment did not abolish the production of lesions, it lessened their duration and extent and rendered them less painful. During the next eight weeks a few small, transient, barely painful, similar sores appeared on the buccal mucosa. Since that time, now five months ago, no fresh lesions have developed.

CASE 2.—J. D., a white boy aged 7 years, was first seen on Sept. 24, 1942. "Canker sores" began to develop one year previously, occurring chiefly on the anterior portion of the tongue. Sites less frequently involved were, in order of their frequency, the sides of the tongue, the inner aspect of the lower lip and, most rarely, the buccal mucosa. About twenty-four hours preceding the appearance of the ulcer the temperature rose to about 101 F. and a dusky red, painful area developed at the site of impending ulceration. Not infrequently during this period there was moderate, painful enlargement of the retroauricular, the anterior cervical and, occasionally, the inguinal lymph nodes, with slight erythema of the overlying skin. Subsidence of the fever and of the enlargement of the nodes rapidly followed the appearance of the aphthae. At the inception of the condition mucosal lesions appeared at intervals of approximately one month and lasted for about one week. The period of freedom from ulcers progressively diminished until, at the time of the first injection of smallpox vaccine, on September 24, they were appearing at the rate of two a week. The second, third and fourth injections were given at intervals of two weeks and the fifth and the sixth injection on November 30 and December 21 respectively. At the last date three lesions only had developed since treatment was begun, and each had arisen about one week after the first, second and third inoculations. They lasted for twenty-four hours, appeared as slightly red, painless

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areas on the tip of the tongue and were unaccompanied by ulceration, fever or adenopathy. The practical freedom of the mouth from lesions allowed a more adequate intake of food, with the result that the general condition improved and the weight increased in two months from 49 to 55 pounds (22.2 to 24.9 Kg.).

SUMMARY AND CONCLUSION

Great improvement occurred in 2 cases of recurrent aphthous ulcers of the mouth and tongue after repeated inoculation with smallpox vaccine. This suggests that such vaccine has a place in the treatment of this disease.

11 Schermerhorn Street.

TEACHING OF OCCUPATIONAL DERMATOSES

JOSEPH V. KLAUDER, M.D.
PHILADELPHIA

The economic importance of occupational dermatoses has been stressed by many writers. Accidental injury occurring in the course of employment represents the most frequent reason for compensation in the United States. The next most frequent reason is occupational dermatoses. The proportion of occupational dermatoses to all other occupational diseases as given by most writers approaches 70 per cent. It is generally stated that occupational dermatoses represent about 10 per cent of all diseases of the skin.

The subject of occupational dermatoses has attained such importance that it is imperative to emphasize it in the curriculum for undergraduate and graduate teaching of dermatology. Pertinent to this discussion are the results of the survey conducted in 1939 by the Council on Industrial Health of the American Medical Association [1] on the status of undergraduate teaching in occupational hygiene in all of the approved four year medical colleges. It was shown in this survey that nearly 60 per cent of recent graduates of approved medical schools are introduced to occupational medicine and surgery early in their professional careers. Information was received from this group of recent medical graduates calculated to determine their appraisal of the adequacy of training in certain components of occupational health. Regarding occupational toxicology, occupational dermatoses, standards of ventilation and illumination, principles of workmen's compensation and casualty insurance relationships, the majority of recent graduates expressed the opinion that these subjects are inadequately treated and in that descending order.

These replies are a direct commentary on the reliability of contributions to occupational health experience provided by unrelated clinical departments without necessary planning and organization. They also refute the attitude that instruction of medical students in occupational health is not practical and that such teaching has no direct bearing on competence in the general practice of medicine.[1]

The survey shows that the average allotment of time devoted to occupational hygiene in medical schools is slightly in excess of five hours. The opinion is expressed that adequate coverage of occupational health is an unusual accomplishment under systems of divided and unrelated responsibility, unless the task of suitable correlation is lodged in one or another of the component teaching units. It is suggested in the report that correlation of this character can effectively be undertaken by those in charge of departments of preventive medicine and public health. This organization of instruction will tend to correct the charges that occupational hygiene is not adequately presented and that instruction is available only as typical cases happen to be encountered in ward or clinic.

It is desirable that separate departments of industrial hygiene be treated in medical schools in order to correlate the teaching of industrial health. In this curriculum, occupational dermatoses should be taught by the department of dermatology, and the instruction should be correlated with the teaching of dermatology.

This paper was written in cooperation with the Council on Industrial Health and the Committee on Industrial Dermatoses of the American Medical Association.

1. Industrial Health: A General Statement of Medical Relationships in Industry Presented by the Council on Industrial Health, J. A. M. A. **114**:573-586 (Feb. 17) 1940.

For the purposes of this study, a survey of medical schools was made by the Council on Industrial Health of the American Medical Association to determine how many of the total hours assigned to teaching dermatology are allotted to teaching occupational dermatoses and to discover whether instruction was provided by teaching divisions other than the department of dermatology.

Information was received from teachers of dermatology in 64 medical schools. Of this number, 35 specified the total hours devoted to teaching occupational dermatoses, including lectures and clinical presentations, to second, third and fourth year classes. In 28 schools the total hours ranged from one to five, and in 4, from six to ten; in 3 the total was more than ten. In 11 of the 35 replies the stated number of hours was estimated, since instruction in the subject was part of general teaching. Only a few replies mentioned that the stated number of hours was devoted exclusively to teaching occupational dermatoses. One such statement is as follows: "The department of dermatology and syphilology, in addition to discussion of interesting occupational dermatoses that are seen at various times in the outpatient department and in the wards, sets aside three hours that are allotted exclusively to occupational dermatoses."

In the remaining 29 replies it was stated that no allotment of time was given to teaching occupational dermatoses (8 replies); that the subject was covered in the general teaching of dermatology, particularly by discussion of contact dermatitis (12 replies); that the subject was taught in the clinic (8 replies). In some schools instruction was contingent on whether cases were available. It was stated in 1 reply that teaching of occupational dermatoses was assumed by the department of preventive medicine in the course on principles and practice of industrial medicine. Such teaching, however, was dependent on whether that course was given.

In 8 of the 64 replies, mention was made of instruction in industrial hygiene given by the department of public health and preventive medicine which included teaching of occupational dermatoses.

The following replies received from different schools are representative: "There are no definite hours for the teaching of occupational dermatoses, as it is an integral part of the general teaching of dermatology in the clinic and in the hospital." "No special lectures are given. Occupational dermatoses are discussed under the general heading of contact dermatitis." "In general, I would say that in teaching of undergraduates 10 per cent of the total time is spent on various phases of industrial dermatoses." "Cases of occupational dermatoses are studied and demonstrated in the dermatologic clinic as they occur." "The subject is taken up with contact dermatitis in one lecture of one hour." "The teaching clinic does not provide enough material." "The state of —— is not highly industrialized." "Since we see so few cases with occupational dermatoses, very little time is spent in such teaching. However, students are instructed in the technic of patch testing and in the various considerations necessary in making a diagnosis of an industrial dermatosis."

From the survey it appears proper to conclude that only in exceptional instances is time allotted to exclusive teaching of occupational dermatoses. The subject is not taught at all (apparently in 12 per cent of 64 medical schools furnishing information), is taught incidentally as part of general instruction in dermatology in lectures and in the clinic or is taught only when cases are encountered in the teaching clinic. As little as one hour is given to the subject, and that in conjunction with the discussion of contact dermatitis. In the opinion of some teachers, paucity of cases of occupational dermatitis is an obstacle in teaching; others apparently question the wisdom of devoting too much time to industrial dermatoses if the medical school is located in a state not highly industrialized.

One reply pertinently stated: "Personally, I do not believe that a course of industrial dermatology separate from the subject as a whole is going to make them as good industrial dermatologists as if they learn their industrial dermatology as part and parcel of general dermatology." I agree with this and also with the comment that instruction in occupational dermatoses is an integral part of the general teaching of dermatology. It is to be noted that there are relatively few occupational diseases of the skin, if one excludes the unimportant occupational stigmas, that present a diagnostic pattern of eruption. The prototype of most occupational diseases of the skin is contact dermatitis, the pattern of which is well known to dermatologists. The cause rather than the type of cutaneous reactions is distinctive. Segregating teaching of occupational dermatoses is not to separate it from the teaching of dermatology. Lectures on occupational dermatoses embrace with few exceptions what is taught in teaching dermatology in general. However, separate lectures on occupational dermatoses furnish a better appreciation of the subject by the student; they afford a more uniform and comprehensive method of teaching, and they emphasize the importance that the subject deserves.

UNDERGRADUATE TEACHING

Teachers of dermatology should have in mind occupational aspects of diseases of the skin when they are giving didactic lectures and clinical demonstrations. In the opinion of some teachers, lack of cases of occupational dermatoses in the clinic is an obstacle in teaching. I believe this implies confusion between occupational diseases of the skin and cutaneous diseases that are compensable under workmen's compensation laws. Such laws are variable in different states. I do not believe it is necessary to demonstrate actual cases of compensable occupational diseases of the skin. Familiarity with the laws constitutes the necessary objective for teaching. As to occupational diseases of the skin, most dermatologic clinics, whether or not they are located in an industrialized region, furnish patients who have cutaneous diseases related to their occupation. For example, contact dermatitis occurs in garage workers and mechanics, who commonly use gasoline or kerosene to clean their hands, in painters, who handle turpentine, and in kitchen workers, soda fountain clerks, housewives and nurses, whose work entails prolonged exposure to soap and water. There are also patients with a variety of dermatoses arising directly or indirectly from trauma and accidental injury.

In addition to the time devoted to the presentation of clinical material, I believe five hours should be devoted to separate lectures on occupational dermatoses. This number of hours is well proportioned in relation to the entire time devoted to teaching dermatology for at least half of the medical schools included in this survey. The reports on 56 of the 64 schools from which information was received mentioned the total number of hours assigned to teaching dermatology. The minimum number of hours was eleven and the maximum one hundred and sixty-five. The following are the percentages of the 56 schools in which various numbers of hours are given to teaching dermatology:

11 to 28 hours	10 schools, or 17.8 per cent
29 to 39 hours	6 schools, or 10.7 per cent
40 to 50 hours	12 schools, or 21.4 per cent
51 to 75 hours	12 schools, or 21.4 per cent
More than 75 hours	16 schools, or 28.5 per cent

In the schools in which the number of hours is less than fifty, the proposed five hours of lectures on occupational dermatoses could be modified to 10 per cent of the

total time given to teaching dermatology. If such allotment, however, is less than thirty hours, it is doubtful that any time could be given to lectures on occupational dermatoses. The following outline of five hours of lectures is suggested:

1 (one hour). Definition and criteria of occupational dermatoses.
Patch tests—diagnostic value, limitations and dangers.
Incidence and economic importance of occupational dermatoses and their relation to workmen's compensation laws.

2 (one hour). Defensive mechanism of the skin.
Contact dermatitis; primary irritant, sensitization dermatitis, cutaneous allergens.

3 (one and one-half hours). Contributory and actual causes of occupational dermatoses.

4 (one and one-half hours). Prevention of occupational dermatoses. Detergents, harmless methods of hand cleansing. Protective clothing and gloves; protective medicinal applications to the skin. Treatment of occupational dermatoses.

In teaching actual causes, one of the following outlines may be used:

1. Chemical, physical and biologic agents causing occupational diseases of the skin. This is the simplest classification of such diseases.

2. Discussion of the occupation or industry causing dermatoses.

3. Discussion of causal factors by groups and of the industry or occupation in relation to these groups.[2] I regard this as the preferable outline, since it affords comprehensive discussion in minimum time.

The following subjects should be correlated with the teaching of occupational dermatoses: principles of workmen's compensation, casualty insurance relationship, the relation of labor unions to industry, prevention of occupational dermatoses so far as ventilation is concerned (dust eruptions), mechanical or closed processes and washing facilities. These subjects should be taught by another department represented in the industrial health curriculum.

GRADUATE TEACHING

The department of dermatology in graduate schools of medicine cannot independently teach all aspects of occupational dermatoses. The desirability of cooperation with the department of industrial hygiene or the department of public health and preventive medicine becomes more emphasized in graduate teaching. The subjects that are related to occupational dermatoses should be taught by one of these divisions. This teaching should include lectures by experts in related fields. An insurance executive is qualified to discuss workmen's compensation laws; a safety engineer is familiar with measures taken to prevent industrial dermatoses, and men engaged in technical fields are equipped to speak on such subjects as, for example, the various types of lubricating oils. Arrangements should be made for attending hearings of an industrial accident board or hearings of claims for workmen's compensation.

It is incumbent on a dermatologist trained in occupational diseases of the skin to recognize the distinctive causes of these diseases through technical knowledge of manufacturing processes and new chemicals used in such processes. This instruction and that in the subjects related to occupational dermatoses are the only necessary additions to the curriculum of graduate teaching of dermatology in general.

Teaching should therefore include visits under proper supervision to industrial establishments in order that the students may become acquainted with technical

2. A study of the actual causes of 527 cases of occupational dermatoses, arranged in groups, is being separately published.

processes, particularly those hazardous to the skin, observe preventive measures, such as washing facilities, and obtain insight to the problem of cleansing the hands. I would suggest the following as a minimum list of the industries to be surveyed: metal working, oil refining, electroplating of metals, printing and engraving, textile and dyeing, manufacturing of chemicals and manufacturing of shoes and leather. In time of war the airplane industry and the industries concerned with the manufacture of explosives and the loading of shells should also be included.

A library of technical books should be available in which there is a representative volume on manufacturing processes. Such a library should also include representative trade journals in which are described new processes, chemicals and compounds. Demonstration of cases of occupational dermatoses is possible through cooperation with clinics maintained by large insurance companies and large industrial establishments and through observation of cases at the time of visits to manufacturing plants.

Occupational dermatoses are of sufficient import to interest industrialists in furnishing endowments in order to create research fellowships in graduate schools of dermatology. Through cooperation with medical directors of different industries full time investigation could be conducted in the plants themselves. There are many investigative aspects of occupational dermatoses. There is need for research on detergents and protective medicinal applications, on the correlation of physiologic states of the skin with the incidence of an occupational cutaneous disease, on the defensive mechanism of the skin and on problems of sensitization and circumstances in which the skin of a worker becomes "hardened" or desensitized to an allergen. Such problems as the pathogenesis of mineral oil folliculitis and the possible correlation of its incidence with the amount of extraneous matter contained in lubricating oil are also worthy of study. The investigation of some of these problems necessitates extensive observation at places of employment.

For the training of physicians in occupational dermatoses Wise and Sulzberger [3] advised the creation of an institute devoted to the diagnosis, treatment, prophylaxis and study of occupational diseases, including diseases of the skin. "It is obvious that such an institute should include a research department, where the scientific study of the diseases may be pursued; and where, more specifically, the question of sensitization and its causes may be investigated with the facilities, time and attention which it deserves."

C. Guy Lane,[4] a pioneer in the field of occupational dermatoses in this country, is director of a graduate course in occupational dermatoses which is planned to occupy one month and is conducted under the auspices of the Harvard School of Public Health. Such a course is conducted with the cooperation of the industrial accident board, the state department of occupational hygiene and the clinics of insurance companies.

Dr. Louis Schwartz, director of the Dermatoses Investigations Section of the National Institute of Health, Bethesda, Md., has conducted pioneer work in occupational dermatoses and has made many valuable contributions. The Dermatoses Investigations Section has a definite relation to the teaching of occupational dermatoses. It is engaged in the investigation of dermatologic hazards in industrial processes in the United States and publishes the results of such studies, as

3. Wise, F., and Sulzberger, M. B.: Industrial Dermatoses, Am. Med. (Spec. Sect.) **39**:4-7 and 16-22 (June) 1933.

4. Lane, C. G.: Occupational Dermatoses: An Educational Program, J. A. M. A. **111**: 1521-1523 (Oct. 22) 1938.

well as bulletins and abstracts from the literature on occupational dermatoses. It also furnishes information to manufacturers, insurance companies, physicians and others.

Dr. Schwartz was in charge of the section's first graduate course on occupational dermatoses, which was held in Bethesda, Md., in August 1942 and consisted of twenty-four hours of lectures [5] in which all phases of occupational dermatoses were comprehensively discussed. The program for the second week comprised visits to six different plants devoted respectively to the manufacture of airplanes, shells, oils, chemicals, explosives and machinery.

Other aspects of teaching of occupational dermatoses include presentation of cases at some of the meetings of the Congress on Industrial Health sponsored by the Council on Industrial Health, symposiums, presentation of cases and exhibits at annual meetings of national societies of dermatology and the work of the National Committee on Occupational Dermatoses, whose membership is recruited from the national societies of dermatology and the consulting staff of the Dermatoses Investigations Section of the United States Public Health Service.

1934 Spruce Street.

5. The outline of these lectures is available for teaching.

EPIDERMOLYSIS BULLOSA

REPORT OF A CASE

CAPTAIN M. H. SAMITZ
MEDICAL CORPS, ARMY OF THE UNITED STATES

Military medicine requires the elimination of the manifestly disqualified. This prevents the possible incapacitation of the soldier and conserves time and energy for the Army. For these reasons the recognition of some of the rare disabling diseases is important. Often they are misdiagnosed and treated as banal conditions. Epidermolysis bullosa falls into this category.

Recently Leider and Baer [1] reported a case in which such an eruption was encountered in a seaman and treated as a fungous infection. The following case was that of a soldier who was treated for allergic dermatitis and pyoderma for nine months. Despite a history pathognomonic of epidermolysis bullosa, he was retained in his assignment in a tank destroyer unit, where the possibility of trauma is ever present.

REPORT OF CASE

W. P. M., an American soldier aged 23, was admitted to the dermatologic ward of the station hospital at Camp Livingston, La., on Jan. 5, 1943, with the complaint of recurrent blisters on the body since infancy. The patient stated that the blisters occurred on any area of the body that had been subjected to trauma. There were no other subjective complaints.

This patient was of German stock and an only child. The only other member of his family afflicted with the disease was his paternal grandfather. The patient was told by his parents that at birth he had two large blisters, one on his wrist and one on his ankle. He was hospitalized twice during childhood for the eruption: at 6 years of age, when he was studied in an attempt to "cure" the disease, and at 10 years of age, when he had scabies and scratched so vigorously that large blisters appeared along the course of the scratch marks. As an adolescent he was annoyed by large blisters on his extremities when he was subjected to the variable degrees of trauma considered a by-product of athletic activities. He noticed that he was able to provoke the formation of vesicles or bullae by pinching or rubbing the skin. The lesions gave rise to no subjective symptoms. In civilian life he was employed as a cashier in a store.

After his induction into the Army an exacerbation of the eruption resulted from the many minor injuries received during the basic training period. Many of the lesions became secondarily infected, broke down as shallow ulcers and healed with some degree of scar formation.

His general appearance was that of a healthy, well nourished young man. Other than the cutaneous changes, there was no abnormality.

The skin showed a large bullous lesion, 1.5 cm. in diameter, on the left wrist. There were two slightly smaller ones on the hands, one on the shaft of the left index finger and one on the ring finger of the right hand. These lesions were tense, and the contents were watery. Two flaccid bullae were present on the right heel. There were numerous crusted lesions on both legs and many pigmented scars on the arms, thighs, legs and abdomen.

When the patient was presented at a clinical meeting of the medical staff of the station hospital he was able to demonstrate the production of a group of vesicles on his abdomen by rubbing his skin.

The results of laboratory studies were within normal limits.

In his report on the histologic examination Captain Robert E. Hobbs stated that sections stained with hematoxylin and eosin showed a slight degree of hyperkeratosis. The epidermis was essentially normal. Areas of separation of the epidermis from the pars papillaris formed

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From the Dermatology Ward of the Medical Service, Station Hospital, Camp Livingston, La.

1. Leider, M., and Baer, R. L.: Epidermolysis Bullosa Hereditaria, Arch. Dermat. & Syph. **46**:419-424 (Sept.) 1942.

small vesicles. There was a minimal infiltration with lymphocytes high in the corium. With Weigert's elastic tissue stain changes in the corium became manifest. The collagen fibers showed a pronounced degree of dissociation. There was a decided diminution in the number of elastic fibers. The areas of separation between the epidermis and the pars papillaris were prominent. The observations were consistent with the diagnosis of epidermolysis bullosa.

COMMENT

The presence of epidermolysis bullosa in the soldier was sufficient grounds for his reclassification. His schooling and background permitted an assignment for limited duty in the clerical field.

SUMMARY

A case of epidermolysis bullosa in a soldier is reported.

Attention is called to the importance of recognizing this rare but disabling disease as a safeguard to the soldier and a saving of time to the Army.

THE PRODUCTION OF BULLAE IN THE SKIN OF THE DUCK

PRELIMINARY REPORT

CAPTAIN I. ARTHUR MIRSKY
MEDICAL CORPS, ARMY OF THE UNITED STATES
AND
LEON GOLDMAN, M.D.
CINCINNATI

Investigations of some aspects of dermatology have been hampered by the lack of an animal whose skin reacts to various irritants with the production of bullae. The guinea pig, which has been employed frequently for studies of eczema, will occasionally acquire subcorneal, intraepidermal (commonest) and subepidermal (rarest) vesicles. These are predominantly microscopic in size and arranged in long fissures, the latter apparently being due to the structure of the skin of the guinea pig. That these vesicles cannot be produced regularly is indicated by Bloch's studies with "primin," an antigen extracted with ether from the fresh leaves of the primrose (Primula obconica).[1] Furthermore, because of their size and shape and the rapidity with which they dry, the contents of vesicles on the skin of the guinea pig are not readily available for analysis.

Goldblatt [2] described an infectious, polymorphous eruption in guinea pigs which had as its most characteristic form a vesiculobullous lesion. Vesicular eczemas in the dog and cat and vesiculobullous lesions in the horse, cow and pig have been described.[3] However, these vesiculobullous forms of cutaneous reactions in animals are rare. Goldschlag [4] reported blisters (size?) on the ears of rabbits following application of vesicants. In addition to the aforementioned animals, the suckling pig [5] has been suggested for the experimental study of vesicles.

The present preliminary report is concerned with the production of serous blisters in the duck. An examination of the literature revealed that feather-bearing animals have received little study from the point of view of the formation of vesicles. Hence we studied the effect of various irritants on the skin of ducks, chickens and owls. The skin of the duck was found most satisfactory for this purpose.

From the May Institute for Medical Research, the Jewish Hospital.

Released for publication by the Air Surgeon, the Gas Casualties Committee and the Advisory Committee on Scientific Publications of the National Research Council, all of which assume no responsibility, other than censorship, for the contents of the article.

1. Bloch, B., and Steiner-Wourlisch, A.: Die Sensibilisierung des Meerschweinchens gegen Primeln, Arch. f. Dermat. u. Syph. **162**:349, 1930.

2. Goldblatt, S.: Ueber einer epidemisch beim Meerschweinchen autretendes infektiöses, polymorphes vorwiegend vesiculo-pustulöses Exanthem, Arch. f. Dermat. u. Syph. **168**:13, 1933.

3. Heller, J.: Die Klinik der wichtigsten Tierdermatosen, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 14, pt. 1. Laporte, O.: Les maladies de la peau du chien, Paris, Les Éditions de l'Éleveur, 1934, p. 70. Bory, L.: Clinique et pathologie comparée, Paris, Masson & Cie, 1939, pp. 7 and 127.

4. Goldschlag, F.: Experiments on the Improvement of the Treatment of Mustard Gas Lesions of the Skin, M. J. Australia **1**:620 (May 30) 1942.

5. Wachtel, C.: Chemical Warfare, Brooklyn, The Chemical Publishing Company, 1941, p. 106.

Microscopically, the normal skin of the duck shows only a thin layer of keratohyalin. The epidermis is thin, in some areas being only one cell layer in thickness and in others three layers in thickness. Slight quantitative changes as regards thickness are found on the legs, thorax and inside folds of the wings. In many places the loose areolar tissue comes directly up to the basal layer of the skin and about the follicles. In other areas, especially about the feather shafts (follicles), dermal tissue may be found as well as heavy collagenous fibers and smooth muscle fibers.

The skin of the duck is extremely sensitive to friction, which produces denudation and bleeding. Microscopic study after friction reveals some crusting, some bleeding into the dermal and areolar tissue and a few hyalin-like masses scattered subepidermally.

The following is a brief summary of the gross and microscopic observations on the plucked skin of ducks exposed to various materials.

1. Intradermal injection of saline solution revealed grossly the immediate formation of a large bullous area. Microscopically, the epidermis showed no changes; in some areas the epidermis was separated entirely by large clear spaces free from fibrin or any reacting cells. Sections examined two hours and ten minutes after injection of saline solution continued to show some of the aforementioned changes.

2. Intradermal injection of water into the skin caused gross changes similar to those produced by injections of saline solution. The microscopic studies were limited to tissue studies immediately after injection of the water and showed changes similar to those with saline solution.

3. Applications of cottonseed oil to the skin produced no gross changes. Microscopically there was slight edema between the epidermis and the dermis; a few inflammatory cells were present.

4. An application of 4 per cent solution of formaldehyde to the skin caused a slight erythema. Microscopically the epidermis was unchanged after one hundred and fifty-five minutes. There was slight edema with scattered infiltration in the derma.

5. An application of 50 per cent croton oil in cottonseed oil produced grossly an erythema-edema reaction followed by large blisters. Microscopically there was little change in the epidermis after one hundred and thirty minutes; below the epidermis were large areas of hyalin-like material with scattered red and white cells and perifollicular infiltrate extending deep into the areolar tissue. After one hundred and fifty-five minutes, there was more intense perivascular and perifollicular infiltrate. The staining qualities of the tissue were poorer. The epidermis was edematous and revealed some vacuolation of cells.

6. An application of 50 per cent mustard oil in cottonseed oil to the skin produced an immediate erythema-edema reaction limited chiefly to areas of application; in about thirty minutes vesicles appeared in parallel rows and the erythema receded. In about one hour after this, new vesicles appeared at the borders of the treated areas. Microscopically, after one hundred and twenty minutes the epidermis was intact and revealed little change; under the epidermis were large masses sharply demarcated and staining like hyalin in certain portions; these collections of fluid involved the areolar tissue and there was a slight perivascular infiltrate. After two hundred and forty minutes, collections of fluid were more prominent and the epidermis was raised high above the adjacent tissue; inflammatory cells made their appearance in these masses. No necrosis of tissue was visible; in some areas the collagenous

tissue fibers were separated by these hyalin-like masses from the main collections; red cells, eosinophils and later fibrin could be found in these collections of fluid.

It may be noted from the preceding observations that the skin of the duck may respond to irritants with the production of bullous lesions. Because of the intimate attachment of the skin about the shafts of the feathers, the vesiculobullous lesions are "held down," as it were, at the corners by the follicular apparatus. However, the individual lesions within the confines of these attachments may reach a large size.

Fluid could be aspirated readily from the large serous areas produced by mustard oil and croton oil. Experiments with various vesicants gave positive results in that large collections of fluid were produced. Analysis of this fluid revealed it to have all the characteristics of blood plasma and to be in equilibrium with the circulating blood plasma. These and other studies will be reported later.

In all of the aforementioned experiments the collections of fluid were entirely subepidermal, the epidermis remaining intact. This can be attributed to the architecture of the skin of the duck. Materials which produce an actual necrosis of the skin (acids) did not produce gross blisters. Burns produced by the application of heat induced necrosis when severe and multiple vesicles when mild.

It was found on repeated experiments that more characteristic blisters are produced in older ducks than in younger ones. Chickens and owls did not show bullous reactions which were as well defined as those in the ducks. However, further studies may reveal methods for producing bullae in these birds.

SUMMARY

The plucked skin of the duck reacts uniformly to some irritants with characteristic large focal collections of serous fluid which can be aspirated. Microscopic studies reveal the blisters to be subepidermal.

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PHAGEDENIC ULCER (PYODERMA GANGRAENOSUM)

TREATMENT WITH SULFAPYRIDINE POWDER AND MOIST CHAMBER THERAPY

A. DOSTROVSKY, M.D.
AND
F. SAGHER, M.D.
JERUSALEM, PALESTINE

For the past decade we have used the term phagedenic ulcer to designate a peculiar type of chronic ulceration of the skin which tends to spread peripherally and is characterized by the presence of certain micro-organisms.

So far, we have had the opportunity of treating 54 patients with this disease; these in the main presented the type of ulceration aforementioned, with involvement of the subcutaneous tissue. The ulcer is irregularly outlined, often crescent shaped. The process may spread in the region of the subcutis and thus undermine the edges of the ulcer and form deep sinuses, over which the overlapping portions of the skin assume a bluish red tinge and surround the ulcer in halo fashion. The surface is uneven and covered with brownish red, smeary matter, exuding a thin, meat-colored fluid. The destructive process spreads rather slowly, as a rule for several months, and usually causes little pain. The regional lymph nodes are not involved. In some of our cases the skin suddenly burst open in the neighborhood of the original ulcer from a subcutaneous tunnel. This was accompanied by violent pain, redness of the skin and a rise in temperature. Such ulcers, only one of which is present at a time, may appear on any part of the skin, preferably, however, over the legs. Healing is slow, and the ulcers are irritable and not amenable to treatment by any of the usual procedures. Surprisingly, in none of our patients did we discover the symptoms of a deficiency disease or any other disorder; only 2 patients had colitis preceding the outbreak of the disease. Improved environmental conditions in the hospital cannot, therefore, account for the therapeutic results referred to later, particularly since half our patients received only ambulatory treatment and remained at home.

As a rule, aerobic, as well as anaerobic, hemolytic streptococci were observed under the overlapping edges of the ulcer, while on the open surface, in the center, Staphylococcus aureus, either alone or in association with Streptococcus haemolyticus or Bacillus proteus, was the most frequent organism noted.

Microscopic examination (11 cases) invariably showed the same changes, viz., necrosis and suppuration, with destruction of the cutis and the presence of nonspecific granulation tissue. The portions of the epidermis overlapping the undermined edges showed hyperplasia. The picture as described is apparently identical with the condition referred to by Brunsting, Goeckerman and O'Leary[1] as pyoderma gangraenosum.

Although the disease is not common, we have had the opportunity of treating rather a large number of patients with the condition, which no doubt indicates a certain prevalence of the disease in Palestine. Twenty-seven patients were

From the Dermatologic Department of the Rothschild-Hadassah University Hospital.

1. Brunsting, L. H.; Goeckerman, W. H., and O'Leary, P. A.: Pyoderma Gangrenosum (Ecthyma): Clinical and Experimental Observations in Five Cases Occurring in Adults, Arch. Dermat. & Syph. **22**:655-680 (Oct.) 1930.

admitted to the department in the hospital with which we are associated, while another 27 were outpatients. Since in the case of the ambulatory patients it was impossible to make all the clinical examinations—as a matter of fact, the visits to the clinic were not regular—the data obtained from this group are included here only so far as they show some parallelism to the data obtained from the hospital patients.

On all patients, in addition to the routine examinations of the stools, urine and blood, determinations of the amounts of uric acid, sodium chloride and dextrose in the blood, as well as the Wassermann and Kahn tests of the blood, were made. For the majority of patients the calcium level of the blood was also determined, and for some the sedimentation rate and the basal metabolic rate as well. Tuberculosis had to be ruled out by tuberculin tests, as well as by roentgenograms of the lungs and the suspected area, and in 1 case several animal experiments were made for this purpose. Since nothing of particular interest was revealed by these examinations, their results are not included here.

It is particularly from the therapeutic standpoint that valuable information may be derived from our material. In the course of the years we have tried almost all the therapeutic methods ever suggested, the trials culminating during the last two years in the adoption of a standard procedure, which has so far produced the most satisfactory results.

Surgical methods of treatment were applied in 10 cases. In 1 of these cases the entire ulcer was excised, together with considerable normal tissue; in the others the undermined edges, including a strip of the surrounding normal skin, were removed, either by scalpel or by diathermy. Plastic operations and transplantations of islets of skin to the affected areas were also tried. In 3 cases sympathectomy was performed (in 2 of them twice). These surgical procedures were not entirely successful. Removal of the affected tissues up to 2 cm. beyond the healthy border, when possible, and thorough cleansing of the surface of the ulcer were indeed effective in the production of healthy granulations, but because of the increased size of the ulcer, epithelization took a long time. Cleansing, moreover, was not always complete, and occasionally after a month or more a new outbreak would occur near the edge or in the center of the ulcer.

The results of sympathectomy were not convincing either. In 1 case a new phagedenic ulcer formed at the site of the operation (inguinal region), which was far larger than the original one. We therefore soon abandoned this method.

Incisions were also restricted to cases in which the process suddenly spread by way of a corridor emerging from the undermined edges. In 1 case such a tunnel 8 cm. long developed; incision, combined with local therapy, produced normal granulation. In cases of this type incision serves the purpose only of immediately opening the anaerobic cavity, which otherwise would burst spontaneously at its peripheral extremity and produce a secondary ulcer.

In accordance with the suggestion of Meleney and Johnson,[2] we used zinc peroxide in 4 cases. Although we strictly observed the authors' prescriptions for this treatment, we were unable to obtain similarly beneficial results, particularly in regard to the progressive tendency of the ulcers. Another great disadvantage is the painfulness of this procedure; so we abandoned it.

When sulfanilamide made its appearance as a therapeutic agent, we thought it worth while to include this newly discovered principle in our therapeutic

2. Meleney, F. L., and Johnson, B. A.: Further Laboratory and Clinical Experiences in Treatment of Chronic, Undermining, Burrowing Ulcers with Zinc Peroxide, Surgery **1**:169-221 (Feb.) 1937.

experiments. There is by no means conformity of opinion as to the effectiveness of sulfanilamide therapy for phagedenic ulcer. This became particularly apparent from the discussion on the occasion of Cipollaro's demonstration [3] of a case before the Manhattan Dermatologic Society (Oct. 8, 1940) and on the presentation of another case by members of the Cincinnati Dermatological Society before the Dermatological Conference of the Mississippi Valley and Central States Dermatological Association.[4]

Recently, an increasing number of good results with sulfanilamide therapy have been reported, but in no instance were they based on material sufficiently large (1 or 2 cases was the rule) to make possible a definite opinion. Montgomery,[5] who used azosulfonamide (the disodium salt of 4-sulfamidophenyl-2″-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonic acid), in only 1 case, recorded no results, while in Weiner's [6] case, in which the disease was particularly severe, sulfanilamide was given by mouth, with excellent results. In the case presented by members of the Cincinnati Dermatological Society the disease was severe, and 6 to 8 Gm. was given a day by mouth, also with cure, though only after seven months. A concentration of sulfanilamide in the blood of 11 mg. per hundred cubic centimeters was achieved in this case; this, on the other hand, was the cause of a number of toxic manifestations, such as a rise in temperature, cyanosis and purpuric eruptions. It was in the discussion of Cipollaro's [3] case that the discrepancies of opinion became particularly apparent. Sharlit suggested chemotherapy; Fox admitted that he had had no experience with sulfanilamide in treatment of this disease; Andrews advocated the combining of chemotherapy with the use of zinc peroxide dressings and roentgen treatment; Costello suggested the application of zinc peroxide paste in combination with the administration of sulfanilamide; Lewis stated that, in his opinion, sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) would not produce the same effect as sulfanilamide. Jacob, in another discussion,[4] reported good results with sulfathiazole in 1 case. The value of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was not discussed on this occasion. For the sake of completeness, Schmidt's [7] suggestion of the use of hyperimmune streptococcus serum for postoperative ulcers must also be mentioned.

Early in the era of therapy with sulfanilamide and its derivatives, we gave sulfanilamide by injection or in the form of compresses. Later we gave it orally, in a total of 13 cases. During recent years we have generally employed sulfapyridine and sulfathiazole in powder form or dissolved in glycerin for local application; here, also, our series represents 13 cases.

To begin with, the results of oral administration of sulfanilamide were not satisfactory. Although on the whole the lesion responded, there were, on the other hand, some cases in which the process progressed during the period of treatment. The quantities administered per day were between 1.5 and 4 Gm., the drug being given for two to six weeks.

The most satisfactory results were those obtained with the use of sulfapyridine or sulfathiazole powder, 0.5 to 2 Gm. per day, in accordance with the size of the

3. Cipollaro, A. C.: Pyoderma Gangraenosum, Arch. Dermat. & Syph. **43**:860 (May) 1941.

4. Pyoderma Gangraenosum, Arch. Dermat. & Syph. **44**:703-705 (Oct.) 1941.

5. Montgomery, W. D.: Pyoderma (Ecthyma) Gangraenosum, Arch. Dermat. & Syph. **40**:924-928 (Dec.) 1939.

6. Weiner, A. L.: Pyoderma Gangraenosum Treated with Sulfanilamide: Report of a Case, Arch. Dermat. & Syph. **41**:711-717 (April) 1940.

7. Schmidt, H. W.: Hyperimmune Streptococcic Serum in Treatment of Pyodermia Gangrenosa Associated with Chronic Ulcerative Colitis and Carcinoma of Colon, Proc. Staff Meet., Mayo Clin. **11**:244-247 (April 15) 1936.

ulcer. Since the pure substance is not available in powder form, we prepared the powder ourselves by grinding the tablets. The treatment was always under strict bacteriologic supervision, as a result of which we can state that when hemolytic streptococci and Staph. aureus were present, the streptococci were the first to disappear, the staphylococci vanishing later. Now and then B. proteus appeared on the scene as an intermediate form, and eventually the ulcers were rendered sterile.

During this stage of the treatment the ulcers themselves were reduced in size, although insignificantly, and assumed a fresher appearance, and the offensive smell disappeared. Purification and a certain amount of shrinking of the edges were also noted, but no considerable stimulation either of granulation or epithelization took place.

Particular attention should be given to introduction of the powder deep beneath the undermined edges, since otherwise there is no contact with the most active portion of the ulcer and the result may therefore be negative. Since this manipulation causes great pain to the patient, we tried instead suspensions of the powder in glycerin, which, however, somewhat hampered the effectiveness of the powder.

The presence in the blood of traces of sulfapyridine, as well as of sulfathiazole, was repeatedly established. From rather a small area and after administration of comparatively small amounts, therefore, the quantities absorbed are sufficiently large to allow chemical determination of the drug in the blood.

In the majority of cases there was a period of several weeks in which streptococci had already disappeared from the surface of the ulcer and staphylococci were left alone on the field, while it was altogether impossible to clear the ulcer of B. proteus. During such periods, however, no progression of ulceration was noted. Since it was impossible to close the cutaneous defect by the chemotherapeutic method alone, other means of achieving this end had to be looked for.

For a considerable period we have used the moist chamber treatment to advantage in stimulating epithelization and granulation in substantial cutaneous defects (e. g., after burns). The defects in the skin are completely covered with straps of adhesive tape, which are left in place for five to seven days. The entire discharge from the surface of the wound is allowed to accumulate there during this time. If the covering loosens in some place through the pressure of the secretion, the break should immediately be repaired with more strips of adhesive, so that none of the secretion may escape. This simple method, which long ago was devised by Bier,[8] but has not found due appreciation in the literature, has proved valuable in the treatment of slowly healing wounds; we tried, therefore, to discover the factor responsible for such satisfactory results. The most obvious assumption is that the secretion which accumulates on the surface of the wound or ulcer provides the stimulating factor. Bacteriologic examination of the matter forming under the cover revealed the presence of a mixed, variable flora. Experiments undertaken to determine the influence of discharges from the wounds on growth of cells in cultures failed, however, owing to the abundance of the bacteria present. We are, therefore, still in the dark as to whether the skin may produce growth-promoting substances. These experiments are being continued along other lines, but it would exceed the scope of this article to report on them in detail.

If moist chamber treatment of phagedenic ulcer is to be successful, the strictest bacteriologic supervision is necessary. In the presence of hemolytic streptococci, the anaerobic conditions created by the chamber promote the spreading of the

8. Bier, A.: Regeneration und Narbenbildung in offenen Wunden, die Gewebslücken aufweisen, Berl. klin. Wchnschr. **54**:201, 1917.

process. Not the slightest evidence of streptococcic infection should, therefore, be found on the ulcer when moist chamber treatment is started. If sulfapyridine treatment has not caused Staph. aureus to disappear, an interval of one week should be allowed, during which the ulcer should be treated with iodoform or, if necessary, with other disinfectants.

After removal of the moist chamber, we found it advantageous to apply compresses soaked in alcohol or in a lead lotion before fixing the moist chamber in place again. Frequently epithelization increases for one to two days after the adhesive bandage has been removed.

After each week of treatment accurate measurements were recorded (in some cases even planimetric measurements were taken) to determine the rate of reduction in the size of the ulcer. We cite the figures for the rate of epithelial growth per week in some of our cases.

With this method of treatment, which has been systematically tried out during the past three years, the ulcer generally healed within three weeks to three months. If the ulcer was treated in an early stage, it healed in three weeks, while for large ulcers which had been present for some time three months was usually required.

We by no means consider the moist chamber treatment a quick method, but we have found it possible to get the process under control soon. The method has another advantage in that it is simple and can be applied to ambulatory patients. What could not be influenced was the tendency of the ulcers to recur, since the scar tissue that forms at the place of the cutaneous defect (usually over the malleolus or the tibia) is, on account of its peculiar location, always exposed to injuries, and thus serves as a locus minoris resistentiae. Further studies will be necessary in investigating the possibility of strengthening the tissues there by plastic procedures or local therapy.

We now report some of our cases, with the measurements of the ulcers. For simplification, the calculations have been made as though the ulcer were rectangular, and the planimetric measurements are not included.

REPORT OF CASES

CASE 1.—A man aged 21 had injured his leg seven years before, when he was riding a bicycle, and an ulcer had developed at the site of the injury. This was treated in the hospital, and healing was obtained in four months. Three years later a similar ulcer appeared on his right hand. On his admission to the hospital we found an ulcer over the right tibia, which had been present for two months. Str. haemolyticus and Staph. aureus were found on the surfaces of the first two ulcers. At the time the patient was suffering from colitis (the bacterial flora being normal). On the third ulcer Staph. aureus and B. proteus were identified. Tests for tuberculosis and syphilis gave negative reactions.

Over the middle of the patient's right tibia there was a typical phagedenic ulcer. The ulcer was treated with sulfathiazole powder until it was rendered sterile. This occurred only after four weeks. Then we started moist chamber therapy, with the results shown in the tabulation.

	Size of Ulcer, Cm.	Defect, Sq. Cm.	Rate of Epithelization, Sq. Cm.
Before treatment	6.5 by 4.3	27.9	...
Second week	4.3 by 4.3	18.5	9.4
Third week	3.5 by 3.4	11.5	7.0
Fourth week	2.7 by 2.1	5.7	5.8
Sixth week	0.2 by 0.3	0.6	5.1

Ambulatory after-treatment was given for two weeks, so that the entire period of therapy was three months.

CASE 2.—A woman aged 31 on admission showed no evidence of internal disease. She had an ulcer over the left malleolus internus, which had been present for seven months and in which anaerobic streptococci and Staph. aureus were identified. All other observations were without significance. Therapy with sulfapyridine powder rendered the ulcer sterile within two

weeks. After this, moist chamber therapy was applied. The patient was then discharged and ambulatory treatment continued, so that the entire period of treatment was one and one-half months.

	Size of Ulcer, Cm.	Defect, Sq. Cm.	Rate of Epithelization, Sq. Cm.
Before treatment	4.2 by 5.4	22.7	...
First week	3.2 by 4.2	13.4	9.3
Second week	2.5 by 3.5	8.75	4.65
Third week	1.2 by 3.0	3.6	5.1

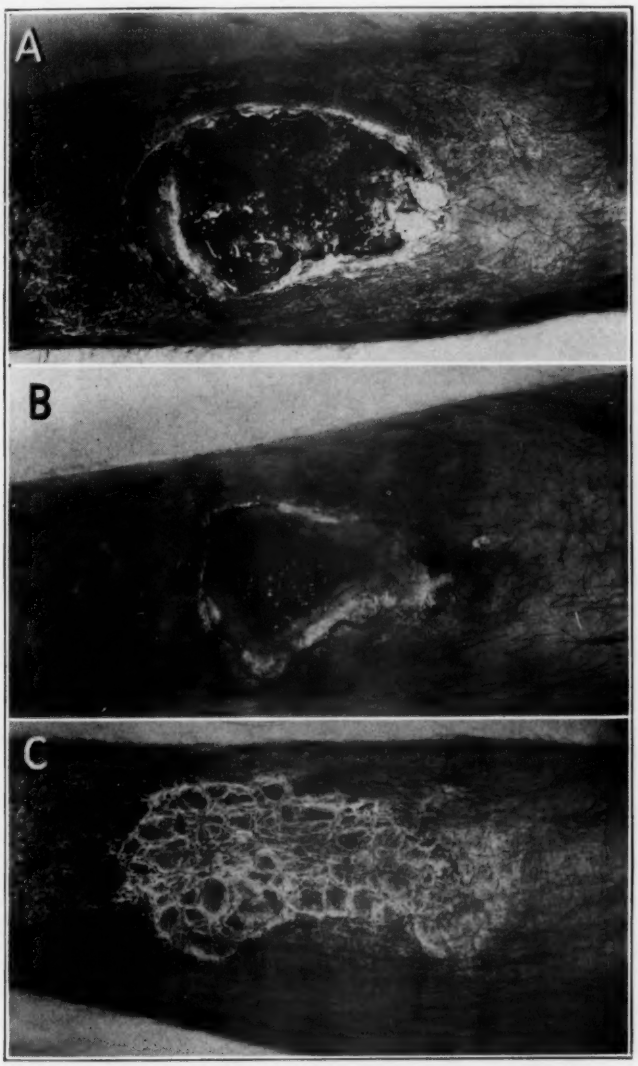

Fig. 1 (case 1).—Typical phagedenic ulcer of the right tibia (*A*), with undermined edges and uneven surface. *B*, appearance of ulcer after treatment with sulfapyridine and sulfathiazole powder and subsequent treatment with the moist chamber for two weeks. Note the reduction in the size of the ulcer, with fresh granulations and active epithelial growth starting from under the entire undermined edge. *C*, genuine scar formation three months after the treatment had been started.

Case 3.—A girl aged 19 years had always been healthy, but five months previous to her admission an ulcer had developed over her left tibia, in which the presence of Str. haemolyticus

and Staph. aureus had been established. Sulfapyridine was applied locally in powder form and was also administered orally, and after two weeks the ulcer was sterile. Then moist chamber therapy was started. The entire period of treatment was two months.

	Size of Ulcer, Cm.	Defect, Sq. Cm.	Rate of Epithelization, Sq. Cm.
Before treatment	10.4 by 9.0	93.6	....
First week	8.4 by 5.0	42.0	51.0
Third week	6.5 by 3.0	19.5	22.5
Sixth week	2.5 by 1.5	3.75	15.75

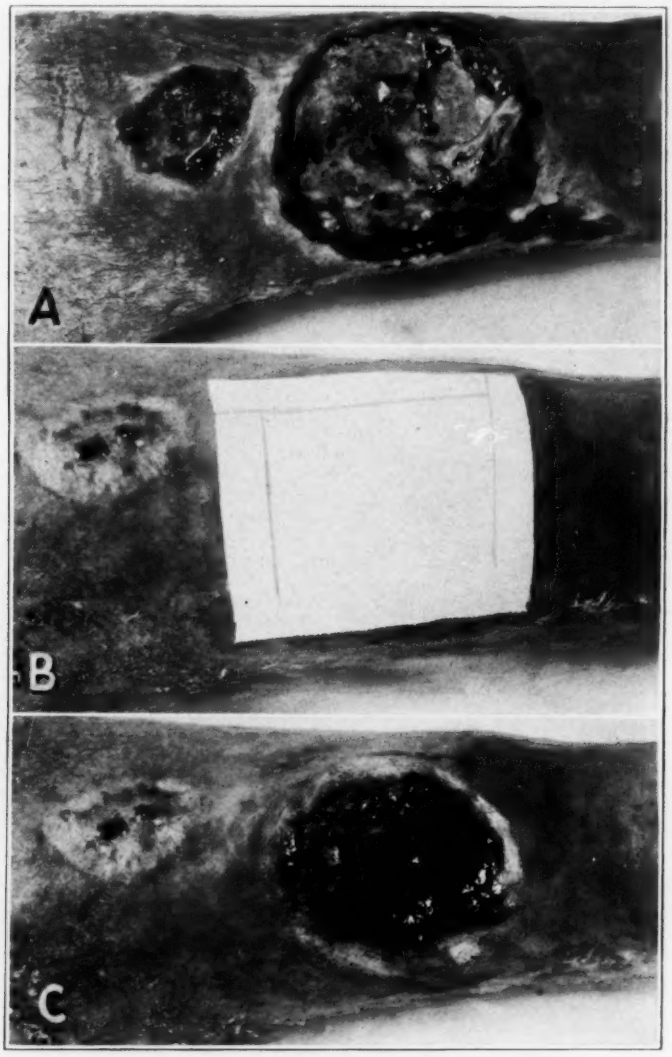

Fig. 2 (case 3).—*A*, phagedenic ulcer, measuring 7 by 7 cm., of the left tibia, with undermined edges, which had been present for a year. *B*, appearance of the ulcer after moist chamber treatment, and *C*, appearance after sulfapyridine treatment and one week of moist chamber therapy.

Case 4.—A woman aged 49 had had an ulcer develop six months previously, over the left malleolus internus, after a mosquito bite. She had never had colitis or any other internal disease before the appearance of the ulcer. Staph. aureus and B. proteus were present. Sulfapyridine powder was applied for a week, after which only B. proteus was still present on

the ulcer. Moist chamber therapy was then started. The entire period of treatment, including the ambulatory period, was one and one-half months.

	Size of Ulcer, Cm.	Defect, Sq. Cm.	Rate of Epithelization, Sq. Cm.
Before treatment	5.0 by 3.5	17.5	....
First week	3.3 by 2.2	7.3	10.2
Third week	2.5 by 1.5	3.75	3.55
Sixth week	1.8 by 1.0	1.8	1.9

CASE 5.—A woman aged 31 had always been healthy except for an anxiety neurosis she had once had. She was admitted to the hospital because of a lesion which was suspected of being a gumma; serologic tests, however, gave negative results. An ulcer on the upper third of her left leg had been present for one and one-half months. In cultures of material from the ulcer we found hemolytic streptococci, Staph. aureus and, later, B. proteus. After treatment with sulfapyridine powder for two weeks only B. proteus was left. Moist chamber therapy was then started. The entire duration of the treatment was two months.

	Size of Ulcer, Cm.	Defect, Sq. Cm.	Rate of Epithelization, Sq. Cm.
Before treatment	5.5 by 5.0	27.5	....
First week	4.5 by 3.3	14.8	12.7
Third week	2.0 by 3.0	6.0	8.8

CASE 6.— A healthy woman aged 25 had undergone an operation for bowlegs three years earlier. After the operation an abscess developed on the right leg, and half a year later an ulcer of the malleolar region appeared. Sympathectomy, performed in the surgical department of this hospital, brought no relief. The patient was transferred to the dermatologic department with an ulcer of three months' duration. Staph. aureus and Staphylococcus albus were identified. To begin with, our treatment consisted of the application of compresses soaked in solution of sulfapyridine for one month. Then followed moist chamber treatment.

	Size of Ulcer, Cm.	Defect, Sq. Cm.	Rate of Epithelization, Sq. Cm.
Before treatment	6.5 by 5.0	32.5	....
Ten days	5.4 by 3.5	18.9	13.6
Three weeks	3.7 by 2.3	8.5	10.4
Four and one-half weeks	2.6 by 1.8	4.7	3.8
Six weeks	1.0 by 0.5	0.5	4.2

After two and one-half months the ulcer had healed. One month later the patient had to be readmitted on account of a recurrent lesion. During the subsequent seven months, which the patient spent in the surgical department, periarterial sympathectomy of the right femoral artery was performed, and transplantations with preputial skin were tried. Later extract of heart muscle eventually effected closing of the ulcer. There has not, however, been sufficient time to judge whether this result may be considered permanent.

CASE 7.—A man aged 35 had eight years previously injured himself while he was riding on a bicycle. Later an ulcer developed over the left malleolus, at the site of the injury. On his admission to the medical department of this hospital, a diagnosis of Buerger's disease was made. In the course of eight years the ulcer had closed four times. Therapy had included plastic operations, sympathectomy, ganglionectomy and adrenalectomy on the side of the ulcer. In addition to treatment with extract of heart muscle, induction of active hyperemia, according to the method evolved by Wilenski, was tried. When the patient was admitted to the dermatologic department, the ulcer had been open again for three months. Bacteriologic studies showed Str. haemolyticus and Staph. aureus. Sulfanilamide was used for ten days, after which moist chamber therapy was started. The entire period of treatment was two and one-half months.

	Size of Ulcer, Cm.	Defect, Sq. Cm.	Rate of Epithelization, Sq. Cm.
Before treatment	2.8 by 4.6	12.9	...
First week	2.5 by 3.8	10.5	2.4
Second week	2.2 by 3.4	7.5	3.0
Third week	2.0 by 3.5	7.0	0.5
Fourth week	1.7 by 3.0	5.1	1.9
Fifth week	1.5 by 2.7	4.05	1.05
Sixth week	1.1 by 1.9	2.09	1.9
Eighth week	0.6 by 1.4	0.84	1.25

COMMENT

As is shown by the data in each case, the increase in epithelization was, on an average, 4 to 7 sq. cm. per week. The last case in our series (that of Buerger's

disease) was an exception, since conditions were particularly intricate and healing, therefore, was much slower. Another exception was case 3, in which, on the contrary, the period of healing was particularly short.

The rate of epithelization depends on at least two factors:

1. The size of the ulcer. The process is naturally more rapid in larger ulcers. Epithelization starts from the edges, and the larger the ulcer, therefore, the longer the epithelium-producing seam. This rapid epithelization does not, however, strike the eye; it is established only by accurate measurements.

2. The site of the ulcer. Lesions developing over the malleolus or the tibia tend to heal more slowly than those in other locations.

A particularly striking feature is the enormous stimulus provided by the moist chamber treatment during the first and second weeks. This is apparently due to the sudden change in conditions.

The data we have presented give an idea of the intricacy of the problem with which the physician is confronted in the treatment of a dangerous ulceration with a tendency to uncontrollable and relentless serpiginous progression. Even radical operation was sometimes unable to prevent the fatal outcome in the presulfanilamide era (3 cases). The introduction of sulfanilamide therapy, however, suddenly changed the situation. After two to three weeks, depending on the location and the size of the ulcer, bacterial activity, as well as further progression of the lesion, is successfully checked; here sulfapyridine powder has proved particularly useful. That this beneficial influence is not due merely to the powder treatment alone, but that sulfapyridine is the active factor in producing the favorable results, is shown by the following experiment: In 1 of our cases an active ulcer was treated with starch alone for five days. This treatment, however, had such a deleterious effect, the lesion progressing while the bacterial flora remained uninfluenced, that we stopped using it and instantly applied sulfapyridine, with the result that the surface of the ulcer was sterilized within ten days. Removal of bacterial growth, however, does not solve the problem entirely; there still remains a lesion which does not tend to heal and has, rather, the appearance of a trophic ulcer. The problem of how to influence this second stage—even after chemotherapeutic procedures have been successful in the first—has been solved by the introduction of moist chamber therapy (fig. 2). With this treatment the surface of the ulcer rapidly fills up; healthy granulations develop; the edges are smoothed out, and rapid epithelization sets in. In cases in which the ulcers are located in the malleolar region, the thin scar tissue is apparently vulnerable and may give rise to erosions, so that plastic operations may become necessary.

SUMMARY

1. Fifty-four cases of phagedenic ulcer (6 of which are reported in detail) form the basis of investigations on new therapeutic possibilities.

2. After several methods of treatment had been tried, the following procedure was used to advantage in a number of cases:

The ulcer was rendered healthy by carefully filling up the entire surface of the wound, particularly the undermined portions of the surrounding skin, with sulfapyridine powder every day.

Moist chamber treatment was instituted.

3. It is shown that with this treatment fresh ulcers healed within two to three weeks and larger and older ones within eight to twelve weeks.

Rothschild-Hadassah University Hospital.

AN APPARATUS FOR THE APPLICATION OF IRRITANT VAPORS TO THE SKIN

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CINCINNATI

Certain investigations that were being undertaken in this laboratory required the development of an apparatus by which vapors could be applied to the skin in a uniform and reproducible manner. None of those previously employed for this purpose or described by others appeared to be satisfactory. Thus Machle and Zwick [1] were interested only in qualitative reactions to gasoline fractions. Their procedure was to fill a series of test tubes about half full with different fractions of the gasoline. These tubes were lined up in a rack, and the forearm of the patient was laid on the open mouths of the test tubes. Miescher [2] used small glass cylinders the bottoms of which fitted into openings in a sheet of celluloid. The top of each tube was closed with a stopper, and just below the stopper was placed a cotton wad which was moistened with drops of the irritating substance or a solution of it. One of these cylinders or a series of them was placed on the dorsal surface of the forearm. In neither of these instances was an attempt made to control the concentration of the vapors by controlling the temperature of the liquid phase. Goldman [3] used a small glass vessel having a ground-in stopper with a small opening in its center. This vessel was held partially immersed in a bottle of water by means of a cork stopper, while the portion of skin to be tested was applied to the small hole in the glass stopper, in contact with the vapors of the substance within the vessel. The two chief difficulties in this procedure were the variation of temperature resulting from the unsatisfactory water bath and the leakage of vapors around the glass stopper. Furthermore, the vapor concentrations could not be determined by analytic means, and therefore reliance had to be placed on calculations derived from vapor pressure curves.

Figure 1 illustrates an apparatus that appears to have surmounted these difficulties. The skin of the patient or animal is applied at point *a*, an orifice 3 mm. in diameter which is closed when not in use by means of a glass stopper ground into place. The irritant liquid substance is introduced through *a* by means of a pipet or medicine dropper drawn out to a fine tip. The liquid is absorbed by the glass wool *c*, which creates a larger surface for rapid attainment of equilibrium between the liquid and its vapor at the temperature used. The cork *b* is lacquered to reduce its porosity to the irritating agents. The wide-mouthed vacuum bottle *d* is filled with water at the desired temperature.

From the Kettering Laboratory of Applied Physiology, College of Medicine, University of Cincinnati.

1. Machle, W., and Zwick, K. G.: Gasoline Dermatitis, M. Bull. Univ. Cincinnati **7**:93, 1935.

2. Miescher, G.: Die Dunstprobe beim Ekzem, Schweiz. med. Wchnschr. **70**:93 (Feb. 3) 1940.

3. Goldman, L.: Personal communication to the author.

Means have been provided for the aspiration of a small portion (5 to 10 cc.) of the vapors for microchemical analysis. This may be done with a gas buret and a sampling tube, as in figure 1, or the vapors may be absorbed in a suitable

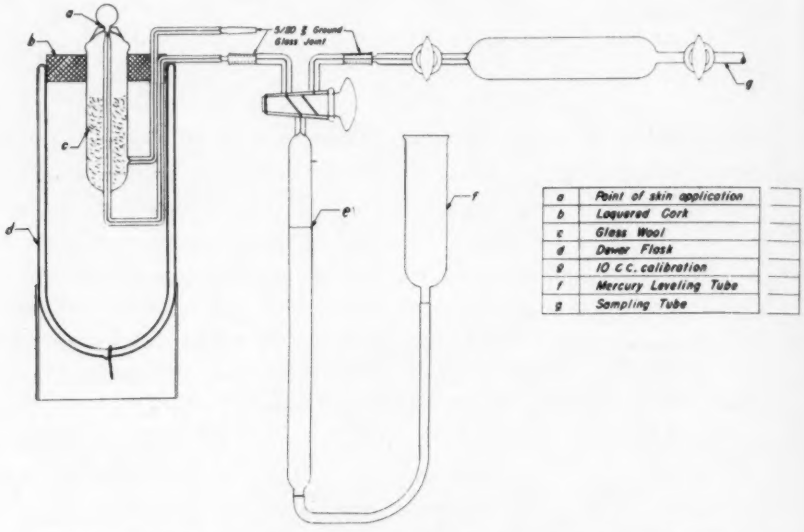

Fig. 1.—Device for applying irritating or toxic vapors to the skin.

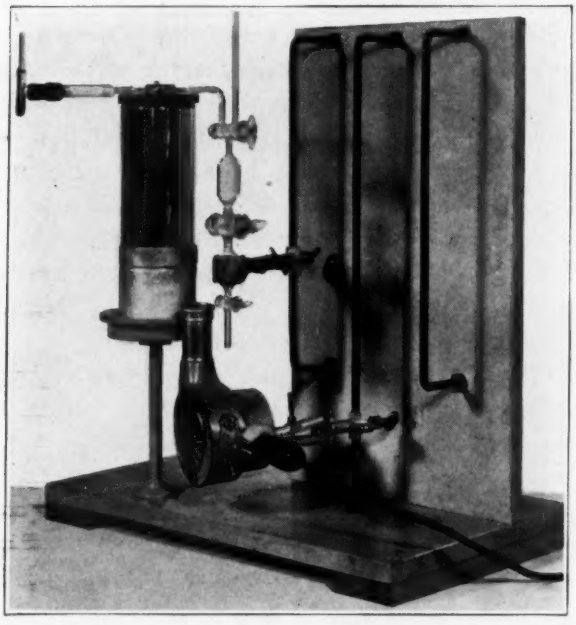

Fig. 2.—Modified device employing an evacuated sampling vessel.

liquid in a small bubble train or spiral absorber after they have been aspirated and their volume measured in the gas buret. An alternative method is illustrated in figure 2. The vapors are drawn into the upper bulb of an evacuated sampling

vessel of known volume. A suitable absorbing liquid is placed in the other bulb. Intimate contact is then obtained by connecting the two bulbs by means of the intervening stopcock and by vigorous shaking. The absorbing liquid and the method of analysis employed are, of course, determined by the nature of the substance used.

Attached to the capillary tube connected with the cutaneous applicator are a calcium chloride tube and a bubble counter. The latter indicates the speed with which the vapor sample is being withdrawn and the completion of the withdrawal. The drying tube is necessary when the substance used is easily hydrolyzed by moisture.

When the water bath of the apparatus is above room temperature it becomes necessary to warm the connecting tube to prevent dewing out of the vapors on the inside of the tube during withdrawal of the sample for analysis. The use

Fig. 3.—Applying irritating vapors to the belly of a rabbit.

of a hair dryer for this purpose is illustrated in figure 2. When the apparatus is being operated above room temperature, much better results can be obtained with it as shown in figure 2 rather than as in figure 1, evidently because of the dewing effect.

Figure 3 illustrates the use of the cutaneous applicator on the shaved belly of a rabbit. In experiments on human beings the forearm is laid across the top of the applicator, with care not to break off the connecting tube.

After standard conditions have been established by analytic means for the operation of this device, a similar device divested of the fragile capillary sampling tubes may be used more conveniently for clinical and experimental purposes.

Donald M. Hubbard made the microchemical analyses.

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LIPOMA-LIKE BASAL CELL EPITHELIOMA

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Pusey [1] gave the only description I have seen of lipoma-like basal cell epithelioma:

> In rare cases, the tubular type of epithelioma develops hypertrophic masses closely resembling lipomata [fig. 1]. These tumors have a pseudo-lobulation, are quite as soft as lipomata, but usually have upon their summits a characteristic epitheliomatous ulcer. The microscopical picture is the usual one of basal cell epithelioma.

"We have seen such a case, lacking ulceration," Sutton and Sutton [2] stated, citing Pusey. It occurred "on the nape of the neck of a man 70 years old. Histologic examination alone prevented error of diagnosis, although the 10 years' duration and the somewhat fibrotic section of the lesion in the gross should have given the hint."

Fig. 1.—"Hypertrophic tumor composed of soft epitheliomatous tissue. Very unusual type of epithelioma. (Author's collection.)" (Pusey,[1] fig. 306, p. 903.)

I [3] published a statistical analysis of 560 basal cell lesions from a series of 1,500 tumors of the skin, 1 of which, the tumor in the present case, was mentioned by Sutton and Sutton.

REPORT OF A CASE

D. A., a white man, an aged farmer, was seen in August 1937 with the complaint of an asymptomatic nodule on the back of the neck. The tumor was 2 cm. in diameter, elevated, sessile, soft and elastic; it was subdermal and seemingly encapsulated and was not tender. The overlying skin was normal, as it usually is in the case of lipoma. The lesion had evolved over a period of at least ten years, enlarging only gradually. The regional lymph

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From the University of Kansas Medical School.

1. Pusey, W. A.: The Principles and Practice of Dermatology, ed. 2, New York, D. Appleton and Company, 1911, p. 901.

2. Sutton, R. L., and Sutton, R. L., Jr.: Disease of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 746.

3. Sutton, R. L., Jr.: Carcinoma of the Skin: Statistical Analysis of Five Hundred and Sixty Basal Cell Carcinomas, J. Missouri M. A. **39**:203-207 (July) 1942.

nodes were normal. These features, in conjunction with the palpable lobulation of the tumor, supported my diagnosis of lipoma. With local anesthesia excision was done, and the wound, closed with horsehair, healed by primary intention. The patient has remained free from recurrence.

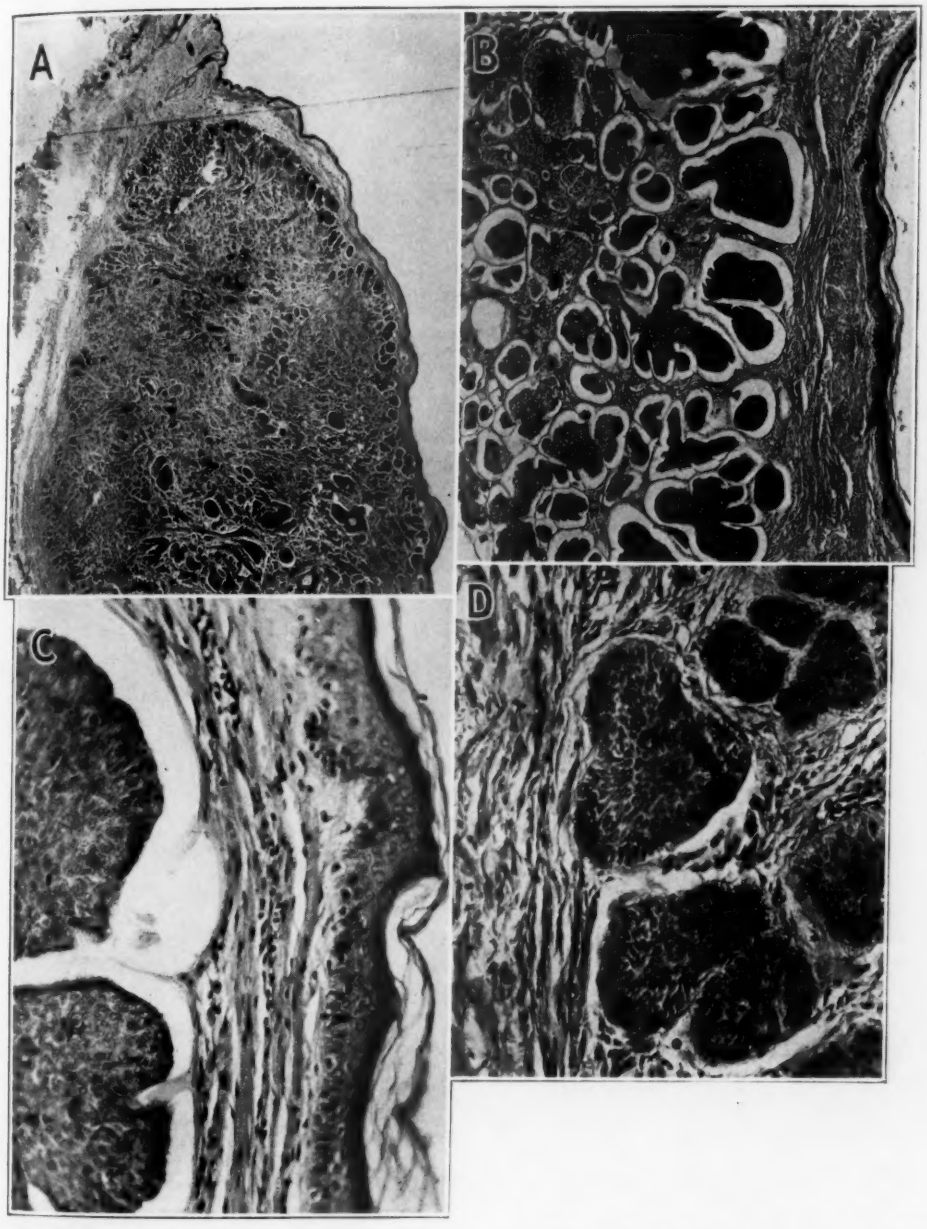

Fig. 2.—*A*, lipoma-like basal cell epithelioma (low magnification of part of section of the whole tumor). *B*, trichoepitheliomatous structure, showing absence of connection of the tumor epithelium with the epidermis. *C*, clumps of tumor cells, typical of basal cell epithelioma, showing relation to the dermis. Retraction is due to fixation. *D*, clumps of tumor cells, showing relation to the encapsulating stroma at the deep boundary of the lesion.

On section, the nodule was seen to be attached to the thin dermis overlying it. The bulging surface was white, not yellow, and was softly fibrotic, not greasy. Microscopic

examination demonstrated a basal cell epitheliomatous structure which simulated that of hair matrix (fig. 2). The lesion might be called a cylindroma,[4] solitary instances of which are recognized. The trichoepitheliomatous structure of some cylindromas has been noted by Weidman [5] and others.

Col. W. F. Harvey, pathologist of the Royal College of Physicians Laboratory, where the whole tumor sections here photographed were made, wrote: "The lesion is a pure basal cell carcinoma of considerable size. There are solid masses and cords of tumor cells with palisaded fringes of cells. There is some hyalinization of the supporting stroma. No connection of the tumor growth with the epidermis is manifest in these sections. There is little lymphocytic reaction and no suggestion of nevus cell growth or of melanoma."

SUMMARY

A case of lipoma-like basal cell epithelioma is reported. Such a case is rare. Clinically the similarity of the tumor to a lipoma is remarkable. Histologically it is of tubular basal cell structure. It is perhaps to be considered a type of cylindroma. It is comparatively benign and may be eradicated by excision.

31 East Sixty-Second Street.

4. Sutton and Sutton,[2] p. 678.

5. Weidman, F. D., in discussion on Binkley, G. W.: Naevus Epitheliomato-Cylindromatosus, Arch. Dermat. & Syph. **37**:289-300 (Feb.) 1938.

MYCOSIS FUNGOIDES

REPORT OF A CASE, WITH CLINICAL, POSTMORTEM AND EXPERIMENTAL OBSERVATIONS

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The following report of a case of mycosis fungoides covers observations extending over nine years. The patient presented cutaneous lesions of the premycotic stage during the first seven years, followed by the tumor stage, which lasted two years, until death.

These observations, together with the histologic picture of the cutaneous tumors, which showed infiltration of pleomorphic cells thought to have originated from the reticuloendothelial tissue of the skin, were considered sufficient evidence for a diagnosis of mycosis fungoides. These features were not sufficient to justify classification of the case as one of lymphoblastoma because the blood count, which was made often (table 1), showed no significant qualitative or quantitative changes in

TABLE 1.—*Studies of the Blood of a Patient with Mycosis Fungoides* *

Date	Red Blood Cells	Hemoglobin, per Cent	White Blood Cells	Polymorphonuclear Leukocytes, per Cent	Lymphocytes, per Cent	Monocytes, per Cent	Basophils, per Cent	Platelets
7/ 3/30	4,500,000	85	9,500	63	33	3	1	..
8/ 2/33	4,100,000	79	8,200	67	30	2	1	..
4/13/36	4,160,000	73	6,150	80	20	..	..	..
10/ 7/37	4,100,000	71	8,800	74	15	3	8	..
8/31/38	2,911,000	60	9,500	71	8	3	18	..
12/15/38	3,090,000	58	12,600	68	31	..	1	107,000

* The Wassermann, Kolmer and Kahn reactions were negative, and the urine was normal.

the white blood cells. Furthermore, no particular involvement of the blood-forming organs was discovered from study of the postmortem material.

This case is reported for the following reasons: 1. It is the first instance of this disease in which the patient was treated with radioactive phosphorus. 2. Passage of tissue from cutaneous tumors through various laboratory animals resulted in infiltrations of a leukemic nature in the livers and spleens of a few mice.

REPORT OF CASE

History and Course.—M. T., a woman aged 50, was first seen in June 1930, with a polymorphous eruption. Some lesions were crescentic and resembled the lesions of erythema multiforme; others were plaquelike, and still others resembled the lesions of psoriasis. They were intensely itchy. The superficial lymph glands were not enlarged. With a series of roentgen ray treatments (multiple exposures to 75 r at weekly intervals), the lesions cleared, and the patient was comfortable for several months. In 1931 and 1932 she had recurrences and consulted other physicians, who gave her injections of neoarsphenamine and more roentgen therapy. In 1933 she returned to my office. The lesions were more indurated at this time, and it was found that 150 r of roentgen radiation was necessary for as satisfactory results as were obtained earlier with 75 r. During the next four years I saw her once or twice a

From the George Williams Hooper Foundation for Medical Research, University of California.

Read before the Section of Dermatology and Syphilology of the California Medical Association at its meeting at Del Monte, Calif., May 2, 1942.

month and gave roentgen therapy to a few lesions here and there, and her disease was kept under control.

In September 1937 tumors began to appear; they broke down and ulcerated, and doses of from 300 to 750 r of unfiltered roentgen rays were necessary for their control. The patient lost weight, and her condition grew worse rapidly. Injections of a bismuth compound and of estrone (theelin) and the administration of sulfanilamide were tried, with no success.

In December 1938, the patient was too weak to get out of bed, and her skin was riddled with tumors. (A check-up on the amount of unfiltered roentgen radiation she had received up to this time revealed a total of 65,300 r.) She was hospitalized, and Dr. John Lawrence,[1] department of medicine of the University of California, was persuaded to give the patient radioactive phosphorus (prepared in the cyclotron). Two millicuries administered by mouth, on December 15, produced considerable improvement in the skin. A similar dose, given on December 30, was followed by more improvement. The smaller nodules seemed to melt away, and the general improvement in the eruption was so remarkable that I believe this therapy should be tried in the future in all cases of this disease, especially in the premycotic stage. The patient died on Feb. 22, 1939, of exhaustion, bronchopneumonia and septicemia.

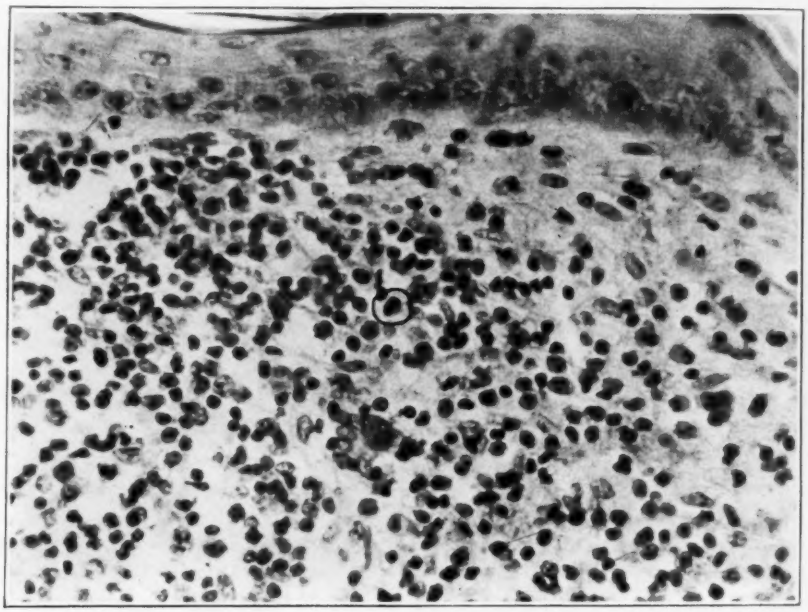


Fig. 1.—Patient's skin, showing nodular infiltration of lymphocytic and mononuclear cells and some mitotic figures (high magnification).

Postmortem Observations (Dr. David A. Wood, professor of pathology, Stanford University).—Anatomic Diagnosis: The diagnosis was: (1) generalized mycosis fungoides of the skin, with infiltration of the breast (cutaneous) and the kidneys; (2) healed pulmonary tuberculosis (primary lesion), with healed tuberculosis of a tracheobronchial lymph node and chronic adhesive pleuritis; (3) moderate arteriosclerosis; (4) pigmentation of the rectum (melanosis coli); (5) bronchopneumonia (the immediate cause of death) and mucopurulent bronchitis; (6) local peritoneal adhesions (pericecal), and mild chronic osteoarthritis of the spine.

The mycosis fungoides was far advanced. The bone marrow was hyperplastic. There were, however, no specific or unusual changes in the spleen, bone marrow or lymph nodes.

Gross Examination: The body was greatly emaciated.

Skin: Many nodular and ulcerated cutaneous lesions, with extensive disfigurement, were noted. Raised, mushroom-like, ulcerated lesions were widely and irregularly scattered in the skin of the head, neck, trunk and extremities. A raised, ulcerated lesion was present in the skin

1. Lawrence, J. H.: Nuclear Physics and Therapy: Preliminary Report on a New Method for the Treatment of Leukemia and Polycythemia, Radiology **35**:51 (July) 1940.

over the ramus of the left mandible. A large, slightly nodular, subscapular lesion on the left side had infiltrated downward into the breast tissue.

Kidneys: The perirenal capsule was flabby. The renal capsule stripped easily, its removal revealing a pinkish brown surface, which was smooth except for remnants of fetal lobulation, and a few small, granular scars of irregular distribution. The kidney measured 12 by 5.5 by 4 cm. The lower pole presented slightly elevated, grayish white nodules, measuring up to 1 cm. in diameter. These nodules were limited strictly to the cortex and stopped abruptly at the medullary portion. The renal pelvis was pale, smooth and glistening.

Microscopic Examination: Skin: The corium and subcutaneous tissue were diffusely infiltrated with tumor tissue, consisting of medium-sized lymphocyte-like cells, with occasional mitotic figures. Scattered throughout the tissue were occasional small, normal-appearing lymphocytes and eosinophils. The cells, however, were only slightly pleomorphic. The overlying epidermis was thin and atrophic. At some distance from the main nodule small groups of similar cells were present in clusters and as diffuse infiltrations of adipose connective tissue (fig. 1).

Breast: The perilobular and interlobular fibrous tissue was coarse and considerably increased. A number of dilated ducts were present. Acinar glandular elements were unusually sparse. Scattered throughout the stroma was a bizarre, irregular infiltration of tumor cells similar to those described in the preceding paragraph. In some areas the cells were dense. Occasional eosinophils and lymphocytes were mixed with the predominating cells.

Kidney: There was moderate capillary hyperemia. Occasional small groups of lymphocytes were situated superficially in the cortex. Near the corticomedullary zone was a poorly defined oval area in which the stroma was infiltrated with oval, moderate-sized, lymphocyte-like cells, a number of which showed mitotic figures. Small lymphocytes were interspersed among these cells.

Bone Marrow: The marrow was cellular, with moderate hyperplasia, which was limited almost entirely to the myelopoietic, or granular, series. Both neutrophilic and eosinophilic myelocytes were numerous. There were occasional mitotic figures in the eosinophilic, as well as the neutrophilic, cells. Megakaryocytes occurred in moderate numbers. Most of the sinusoids were distinctly visible. Their lining reticuloendothelial cells were frequently prominent and appeared slightly swollen. Normoblasts and nucleated red blood cells were occasionally seen. These, however, were sparse as compared with the granular cell constituents. In some of the more cellular areas giant, plasma-like cells occurred in small numbers and in rather scattered distribution. These cells possessed small round, somewhat eccentric nuclei. The chromatin, even though clumped, did not show the classic spokelike arrangement characteristic of the typical small plasma cell. The cytoplasm of these cells was finely granular, almost slate colored and slightly eosinophilic. Lymphocytes were extremely infrequent, and when present occurred in vascular spaces. Sections of bone marrow from the rib, sternum and vertebra revealed no areas of tumor cell infiltration, such as were noted in the kidney and the skin. There were no striking changes in the reticuloendothelial apparatus.

EXPERIMENTAL STUDY

A cutaneous (nonulcerated) nodule was removed aseptically. Grafts prepared from part of it were placed under the skin of 2 guinea pigs and 4 mice, with negative results. The other part was emulsified with saline solution. Inoculation with this emulsion of tubes containing brain broth and of others containing Sabouraud's medium yielded no growth. Inoculation of blood plates resulted in a growth in twenty-four hours of organisms which were identified as Bacillus proteus and Bacillus coli.

The emulsion was injected into 6 mice (3 intraperitoneally and 3 intracerebrally). Ten months later 1 of the mice which was inoculated intraperitoneally and 1 which was inoculated intracerebrally showed evidence of leukemic infiltration in some of their organs, especially in the liver and spleen.

Mouse to mouse transfer, for three passages, was made over a period of three years, and before the experiment was terminated chorioallantoic membranes were inoculated and the results recorded.

Microscopic examinations of the mouse tissue were made by Dr. James Rinehart, professor of pathology, University of California Medical School.

Complete blood counts made on several of the mice revealed nothing significant.

Details of the mouse experiments (preliminary report) follow.

Dec. 4, 1939: Mouse 3 died (inoculated intracerebrally on Feb. 22, 1939). Its liver and spleen were greatly enlarged and showed many macroscopic nodules. Microscopic examination of the liver showed moderate infiltration of the sinusoids with lymphocytic and mononuclear cells. Large oval nodules of densely grouped similar cells were also present (fig. 2). The

spleen contained many large nodules composed of oval mononuclear cells, similar to those seen in the liver. Mitotic figures were numerous. The intervening pulp showed distinct structure, with small groups of similar cells.

An emulsion of liver, spleen, brain and lymph glands from mouse 3 was injected intraperitoneally into 4 mice (3A, 3B, 3C and 3D), with the following results (the word "positive" indicates a microscopic picture similar to the original):

Mouse 3:
Died 12/4/39
Positive

Mouse 3A:	Mouse 3B:	Mouse 3C:	Mouse 3D:
Died 4/27/40	Died 7/29/40	Died 9/19/40	Died 9/19/40
Negative	Negative	Positive	Positive

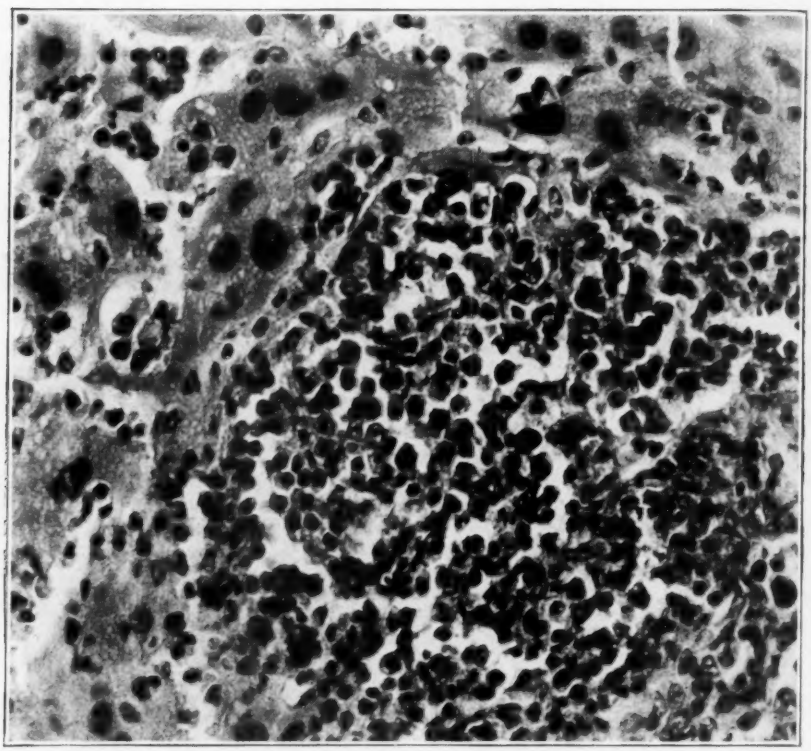


Fig. 2.—Liver of mouse 3, showing portion of the nodular infiltration (× 415).

Sept. 19, 1940: Mouse 3C and mouse 3D had been dead for several hours. The liver and spleen from mouse 3C were emulsified and the emulsion injected subcutaneously into 6 mice (3C1, 3C2, 3C3, 3C4, 3C5 and 3C6) and intracerebrally into 6 mice (3CA, 3CB, 3CC, 3CD, 3CE and 3CF). Most of these mice died within twenty-four to seventy-two hours, undoubtedly as a result of the postmortem contamination of the organs used in the emulsion. Mouse 3C5 and mouse 3CE, the only animals which survived, were killed on April 4, 1941 and their organs found to be normal.

Dec. 16, 1939: Mouse 4 died (inoculated intraperitoneally on Feb. 22, 1939). Its liver and spleen were greatly enlarged, but no macroscopic nodules were seen. Microscopic examination of the liver showed many mononuclear and polymorphonuclear cells in the sinusoids, a "leukemoid" reaction. The spleen was hyperplastic, and microscopic examination showed some giant cells and foci of nucleated red blood cells. The kidney showed lymphoid nodules, which were larger than normal.

An emulsion of the liver, spleen and kidney from mouse 4 was injected intracerebrally into 4 mice (4A, 4B, 4C and 4D).

Dec. 3, 1940: Mouse 4B died (inoculated intracerebrally on Dec. 16, 1939). Its liver and spleen were enlarged but showed no macroscopic nodules. Microscopic examination of the liver showed considerable periportal infiltration of lymphocytic and mononuclear cells. The spleen was enlarged and contained small groups of oval mononuclear cells with mitotic figures (fig. 3). In the kidney there were one large and several small foci of infiltration, resembling leukemic lesions. (fig. 4).

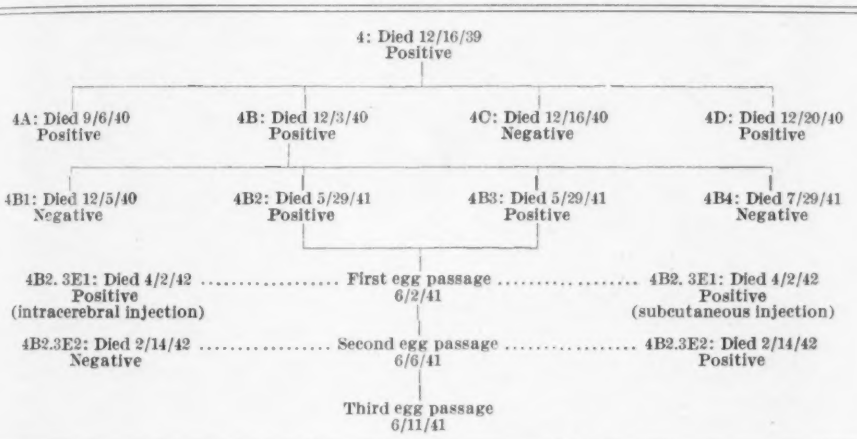
An emulsion of the liver, spleen and kidney from mouse 4B was injected subcutaneously into 4 mice (4B1, 4B2, 4B3 and 4B4) and intracerebrally into 4 mice (4BA, 4BB, 4BC and 4BD). All animals of the latter group died within a few days.

May 29, 1941: Mouse 4B2 and mouse 4B3 (inoculated subcutaneously on Dec. 3, 1940) were sick. Both were killed, the tissues examined histologically and their organs used for egg and animal passage. Their livers and spleens were enlarged and showed the type of infiltration previously described.

An injection of 2 cc. of an emulsion of these organs in saline solution was made into the chorioallantoic membranes of 2 eggs 8 days old.

June 2, 1941: Four days later 1 of the eggs showed several small pinhead-sized, brownish black areas in the membrane. The entire membrane was removed and emulsified, and 2 new eggs and 4 mice (2 subcutaneously and 2 intracerebrally [4B2.3E1]) were inoculated with this material.

TABLE 2.—*Results* of Mouse to Mouse Passage and Inoculation of Chorioallantoic Membranes*



* The word positive indicates a microscopic picture similar to the original.

June 6, 1941: Four days later the membranes of both eggs of the second egg passage showed several brownish black areas, such as were described in the report of the first egg passage. One of these membranes was placed in Zenker's solution and sections prepared.

Microscopic examination of these sections showed lesions in the chorioallantoic membrane, involving the epithelium and the deeper layers. There were necrosis of the superficial layers and proliferation about and below the necrotic part. In many places the proliferation took the form of pearls and long finger-like processes. This is typical of the so-called pock lesion which forms on the membrane from injury by any of many agents. It may be the result of a virus, of trauma by the needle when the shell membrane is opened or of shell dust or unsedimented particles of sand or abrasives used in grinding the inoculum.

The other chorioallantoic membrane was emulsified, and 2 new eggs, 2 tubes of brain broth and 4 mice (2 subcutaneously and 2 intracerebrally [4B2.3E2]) were inoculated with this material.

June 11, 1941: Five days later the membranes of both eggs of the third egg passage showed the same brownish black lesions. The membranes were again emulsified for egg passage. No mouse transfer was made.

June 16, 1941: Both membranes of the fourth egg passage were clear.

April 2, 1942: Mice 4B2.3E1 (inoculated subcutaneously and intracerebrally on June 2, 1941; first egg passage) were killed for examination of tissue. Their livers, spleens and kidneys showed a leukemic type of infiltration.

Feb. 14, 1942: Mice 4B2.3E2 (inoculated subcutaneously and intracerebrally on June 6, 1941; second egg passage) were killed and their tissues examined. The livers, spleens and kidneys of the mice inoculated subcutaneously presented a positive histologic picture (similar to the original) and the organs of the mice inoculated intracerebrally a negative picture.

From Dr. Rinehart's report, as well as from examination of the slides themselves, there is no doubt about the character of the infiltration in certain organs of the mice used in this experiment. The picture was more striking in the mice of the first passage, but the same leukemic type of infiltration, though not so intense, was present in the livers, and occasionally in other organs, of the mice used in the several passages.

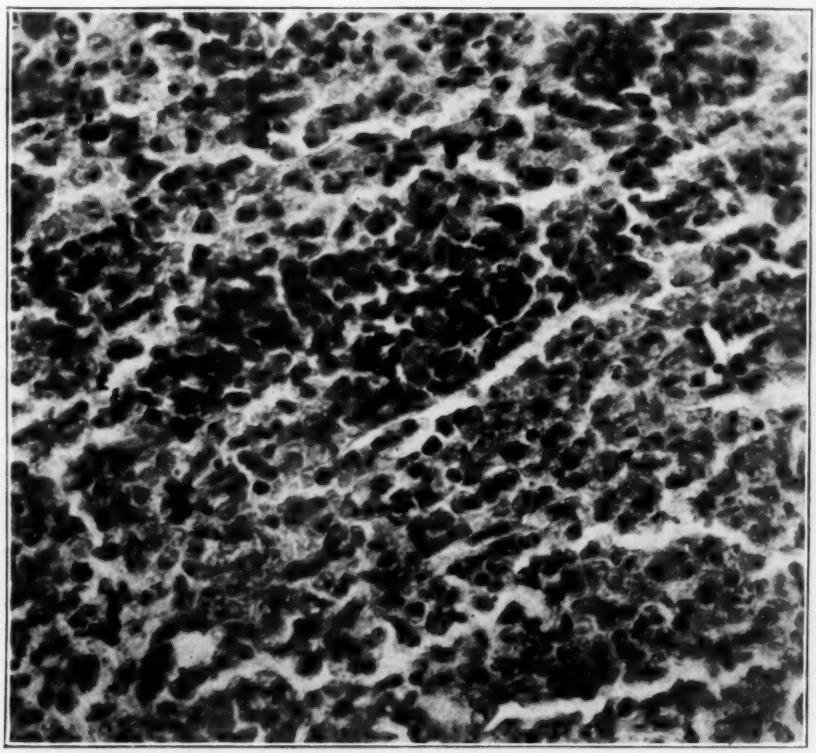


Fig. 3.—Spleen of mouse 4, showing scattered foci of oval mononuclear cells, several of which have mitotic figures (× 415).

For comparison, sections of organs from normal mice were examined, as well as sections from 4 mice infected with syphilis which had been kept under the same environmental condition as the mice with mycosis. Dr. Rinehart's notation on one of the last-mentioned mice is interesting: "The liver and spleen showed a leukemoid reaction similar to that seen in some of the mice with less definite mycosis."

What interpretation can be placed on these observations? I could find no references in the literature to a successful transfer to animals of diseases of human origin belonging to the lymphoblastoma group. There were no references to experimental work on mycosis fungoides. There were, however, numerous references to the leukemias in animals. Inasmuch as these two diseases under certain conditions have been classified under the general term of lymphoblastoma, I used the animal experiments on leukemia as a theoretic guide in analyzing the results.

Richter and MacDowell reported on a spontaneous leukosis which occurs in certain inbred strains of mice.[2] It can be transferred by mouse to mouse passage, with nearly 100 per cent takes, the white blood cell count becoming leukemic in type and infiltrations and tumors occurring in the organs. In mycosis fungoides, however, the white blood cell count is usually of aleukemic type, as it was in my patient and in the mice checked on in the experiments. Therefore the blood counts were of no comparative value. The strain of mice employed in my experiments was that commonly in use at the Hooper Foundation, known as the Cook strain, and Dr. Karl Meyer stated that he had never encountered spontaneous leukosis in this stock.

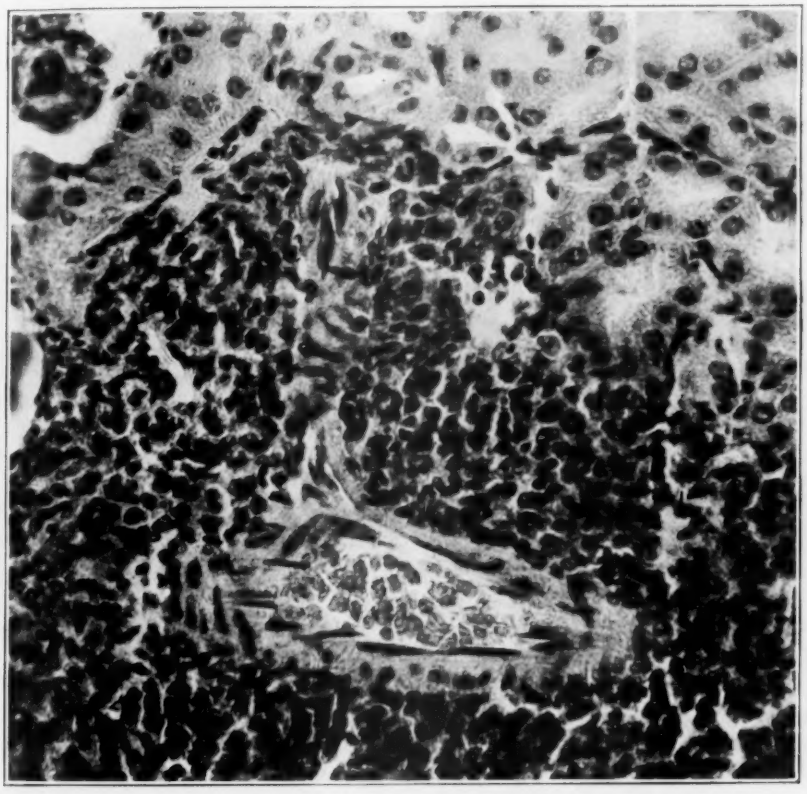


Fig. 4.—Kidney of mouse 4B, showing portion of the nodular infiltration around the blood vessel (× 425).

Emmel[3] claimed to have induced a "leukosis complex" in the chicken, dog, monkey, hog, goat and sheep by injecting bacteria of the paratyphoid and typhoid groups. In the present experiments it is to be noted that the blood plate culture of the emulsion of the original tumor tissue showed the presence of B. proteus and B. coli. The blood plate cultures made from the emulsions of the mouse organs at the time of the various animal transfers, however, were sterile except in the few instances in which death had occurred several hours prior to transfer.

2. Richter, M. N., and MacDowell, E. C.: Studies of Leukemia on Mice: I. The Experimental Transmission of Leukemia, J. Exper. Med. **51**:659 (April) 1930.

3. Emmel, M. W.: The Etiology of Fowl Paralysis, Leukemia and Allied Conditions in Animals, Technical Bulletin 305, University of Florida, College of Agriculture, Agricultural Experiment Station, 1936.

In reviewing the literature, one finds that leukosis has developed in mice after the injection of certain chemicals, such as the dibenzanthracenes,[4] and after the prolonged injection of estrogens.[5]

COMMENT

In view of the observations described and those of other investigators working with mice, it would be a mistake to place too much importance on the results of these experiments. However, the circumscribed nodules seen even macroscopically in the livers and spleens of the mice in the first transfers were practically identical with the nodules observed in the skin and kidneys of my patient.

Three questions come to my mind. 1. Was the injection into these mice of an emulsified tumor of mycosis fungoides the cause of the leukemic type of infiltration seen in their livers and spleens? 2. If so, was the reaction a foreign body response, or had it a specific cause? 3. If the reaction had a specific cause, was the causative agent a malignant tumor cell, a virus or a toxin?

Ewing [6] stated the belief that mycosis fungoides is a reticulum cell lymphosarcoma, originating from the reticuloendothelial cells. Fraser [7] agreed with Ewing and expressed the opinion that the disease is neoplastic, and not inflammatory even at the beginning. He stated that the inflammatory reactions observed during the premycotic stage are due to the development of tumor cells. Experimental investigations have shown that leukemia in the mouse, guinea pig and squirrel (three separate species) can be transmitted by the injection of emulsified leukemic tissues or cells, but not by filtrates containing noncellular agents.

In fowls, however, Lee and Wilcke [8] have shown that leukosis can be transmitted by injection of cell-free filtrates of infected chicken tissue and that the injection of a filtrate of tissue infected with one type of leukosis apparently produces all the various types considered as an expression of this disease, i. e., neurolymphomatosis gallinarum, associated with ocular lesions, hemocytoblastosis and lymphoid, erythroid and myeloid leukosis. They stated the belief that the causative factor in the filtrate of fowl leukosis–infected tissue is a virus, since its behavior is similar to that in electrophoresis experiments. There are other investigators, however, in whose opinion the etiologic agent in the filtrate is a toxin, not a virus.

It was observed in our experiments that the inoculation of chorioallantoic membranes of 8 day old eggs with emulsions of mouse organs from the third mouse passage resulted in perpetuation of the leukemic infiltration–producing substance (when the emulsified membrane was injected into mice four days later). Storti and Mezzadra [9] attempted to culture the virus of fowl leukemia on chorioallantoic membrane, but the results of their experiment are not known, as their article is not available.

Another interesting observation in my experiments was the long period of incubation between the time of inoculation and death (an average of ten months). Mice in the same room infected with syphilis lived an average of two years. In the

4. Burrows, H., and Cook, J. W.: Spindle-Celled Tumors and Leucaemia in Mice After Injection with Water Soluble Compounds Composed of 1:2:5:6-Dibenzanthracene, Am. J. Cancer **27**:267 (June) 1936.

5. Lawrence, J. H., and Gardner, W. U.: Transmissible Leukemia in the "A" Strain of Mice, Am. J. Cancer **33**:112 (May) 1938.

6. Ewing, J.: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922, p. 382.

7. Fraser, J. F.: Mycosis Fungoides: Its Relation to Leukemia and Lymphosarcoma, Arch. Dermat. & Syph. **12**:814 (Dec.) 1925.

8. Lee, C. D., and Wilcke, H. L.: Migration of Etiologic Agent of Fowl Leukosis When Subjected to Electrophoresis, J. Am. Vet. M. A. **94**:178 (March) 1939.

9. Storti, E., and Mezzadra, G.: Attempts to Culture Virus Fowl Leukemia on Chorio-Allantoic Membrane: Preliminary Report, Sang **12**:533, 1938.

susceptible C58 mouse strain reported on by MacDowell and Richter,[10] all the mice, with rare exceptions, died of leukemia within two weeks of inoculation, and Seibold, Rathbone and Furth [11] were able to make an otherwise leukemia-resistant strain of mice susceptible for forty-two days by treating them with 200 r of unfiltered roentgen rays.

RECOMMENDATIONS

In spite of the inconclusive nature of these experiments, it is the opinion of those who have contributed to and/or criticized this study that as other cases of mycosis fungoides become available similar experiments should be made. In addition to normal mice, mice devitalized by a preliminary dose of roentgen radiation should also be included in such a study. More frequent studies of the blood should be made. Filtrates of infected organs should be injected and results compared. The studies on inoculation of chorioallantoic membranes should be extended.

SUMMARY

A case of mycosis fungoides was observed for nine years, until death. At autopsy, in addition to the cutaneous tumors, nodules similar to those in the skin were observed in the kidney.

One of the cutaneous nodules was emulsified and the emulsion injected intraperitoneally and intracerebrally into mature white mice. Ten months later some of the mice showed nodular infiltrations of a "leukemoid" type in the livers, spleens and kidneys.

Mouse to mouse transfers, with an emulsion of the involved organs, were successfully made for three passages. At the end of this time, and before the experiment was discontinued, the infiltration-producing substance was perpetuated on chorioallantoic membranes for two passages.

10. MacDowell, E. C., and Richter, M. N.: Studies in Mouse Leukemia: Hereditary Susceptibility to Inoculated Leukemia, J. Cancer Research **16**:3 (Aug.) 1930.

11. Seibold, H. R.; Rathbone, R. R., and Furth, J.: Studies in Transmissible Lymphodenesis of Mice, Proc. Soc. Exper. Biol. & Med. **29**:629 (Feb.) 1932.

EFFECT OF ESTRADIOL LOCALLY APPLIED TO ABNORMAL SKIN

HANS SELYE, M.D., PH.D., D.Sc., F.R.S.(C.)
MONTREAL, CANADA

The fact that natural folliculoids,[1] such as estradiol or estrone, and artificial folliculoids, such as stilbestrol, are effectively absorbed through the skin has been demonstrated by numerous investigators.[2] It has been found, for instance, that in the mouse inunction of the skin with solutions or suspensions of folliculoid compounds causes typical estrous-like changes in the internal sex organs. Although it has often been claimed that in certain cases folliculoids may act as carcinogens, none of the aforementioned investigators were able to produce cutaneous changes resembling cancer by the local application of the folliculoids to the skin.

That folliculoids may elicit some local action on the skin has been shown by Steinach,[3] who found that cutaneous hyperemia may be induced by such compounds in the rat. Argüello [4] observed, in the same species, great diminution in the number of hair follicles and hyperplasia of the cornified layer after subcutaneous injection of estrone. Although these changes were greatest in the region immediately surrounding the site of injection, he did not consider them the direct effect of the endocrine substance, since local application of estrone to the skin had no effect. He expressed the belief that they were more probably due to an alteration in the pituitary. On the other hand, Kun [5] reported that the percutaneous administration of estradiol or its benzoate in an ointment, in addition to causing hyperemia of the skin, stimulates the growth of hair in infantile or senile rats, hair growth in which is normally poor. Histologically there is thickening of the skin, with cellular proliferation in the epidermis and in the connective tissue of the corium. The hair follicles, the sebaceous glands and the cutaneous muscles all show an increase in size.

Previous observations [6] showed that squamous cell metaplasia and "precancerous" changes are most readily produced in rats after local injection of follicu-

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From the Department of Anatomy, McGill University.

1. The term folliculoid is used to designate substances having an activity resembling that of the ovarian follicles (Selye, H.: Pharmacological Classification of Steroid Hormones, Nature, London **148**:85, 1941).

2. Glimm, E., and Wadehn, F.: Beitrag zur Kenntnis eines Sexualhormons der menschlichen Placenta (Feminin), Biochem. Ztschr. **179**:3, 1926. de Jongh, S. E., and Laqueur, E.: Ueber die percutane Wirkung des Menformons, Acta brev. Neerland. **2**:220, 1932. Burrows, H., and Kennaway, N. M.: On Some Effects Produced by Applying Oestrin to the Skin of Mice, Am. J. Cancer **20**:48, 1934. Emmens, C. W.: The Inunction of Sex Hormones on the Skin, J. Endocrinol. **2**:368, 1941. Palmer, A., and Zuckerman, S.: Further Observations on the Similarity of Stilbestrol and Natural Oestrogenic Agents, Lancet **1**:933, 1939.

3. Steinach, E.: Zur Geschichte des männlichen Sexualhormons und seiner Wirkungen am Säugetier und beim Menschen, Wien. klin. Wchnschr. **49**:161, 1936.

4. Argüello, R. A.: Influence de l'administration prolongée d'oestrone sur la peau annexes du rat blanc, Compt. rend. Soc. de biol. **124**:497, 1937.

5. Kun, H.: Wirkungen des Follikelhormons auf die Haut bei perkutaner Verabreichung. Histologische Untersuchungen an infantilen und senilen Ratten, Wien. klin. Wchnschr. **50**:408, 1937.

6. Selye, H.; Thomson, D. L., and Collip, J. B.: Metaplasia of Uterine Epithelium Produced by Chronic Oestrin Administration, Nature, London **135**:65, 1935.

loids into the uterine lumen, an observation which has repeatedly been confirmed [7] and which implies that such local treatment may also lead to pathologic types of keratinization in the skin. In view of the fact that folliculoids are frequently used as ingredients of ointments for the skin, it appeared desirable to reinvestigate this problem.

A few years ago Howard,[8] working at McGill University, described the so-called rhino mouse, which bears the allele of the gene for the hairless mouse. In this animal the skin is almost completely hairless and greatly thickened, as well as increased in total area. As a result of this, deep, thick folds of skin cover the surface of the animal, so that its appearance justifies the name given it. This cutaneous abnormality is a simple recessive characteristic, heterozygotes being completely normal and the second filial generation showing a 3:1 ratio of normal and rhino rats. The histologic structure of the skin will be described in detail in the doctor's thesis of Mr. F. C. Fraser, of the department of genetics; so I shall limit myself to a few statements which are essential to the understanding of the results obtained. The skin of the heterozygotes is, as was said, macro-

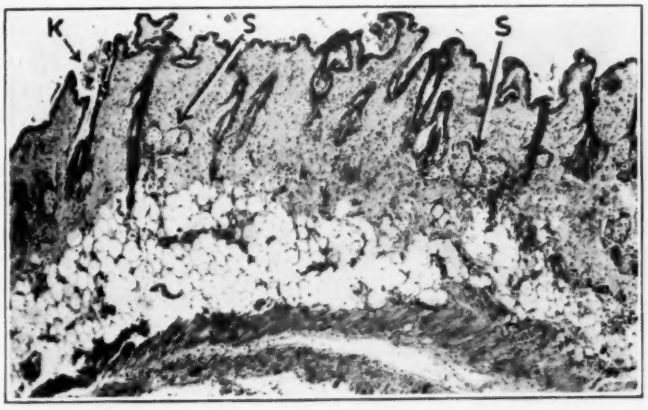

Fig. 1.—Section through the skin of a heterozygote mouse in which the rhino type of skin was not manifest. The general histologic appearance of the skin is also normal, although an abortive beginning of excessive keratinization can be distinguished in occasional hair follicles, such as that marked *K*. The sebaceous glands are indicated by *S*.

scopically normal and covered with fur. Histologic examination does not reveal any major abnormality, although occasional hair follicles are filled with more or less irregular clumps of keratinized squamous epithelium. In contrast, the skin of rhino mice contains almost no normal follicles, and the derma is filled with large cystic spaces, most of which contain amorphous detritus. Few of these cysts are filled with well preserved cornified squamous cells, and some of them have close topographic connections with sebaceous glands, the secretions of which are discharged into the cysts. By following the evolution of these changes, especially in young animals, in which the condition is not as yet fully developed,

7. Arnold, O. H.; Grumbrecht, P., and Loeser, A.: Organveränderungen und Allgemeinreaktion bei intrauteriner Anwendung von oestrogenen Substanzen, Arch. f. exper. Path. u. Pharmakol. **191**:192, 1938. Grumbrecht, P., and Loeser, A.: Aufbau der Uterusschleimhaut bei intrauteriner Einwirkung von oestrogenen Substanzen, Arch. f. Gynäk. **167**:373, 1938; Die innersekretorische Bedeutung des Uterus, ibid. **168**:889, 1939.

8. Howard, A.: "Rhino," an Allele of Hairless in the House Mouse, J. Hered. **31**:467, 1940.

one may easily ascertain that the cysts are actually distended hair follicles in which the hair itself has undergone almost complete degeneration. The wall of the cyst continues to form amorphous material, which is only incompletely extruded and, together with the sebaceous secretion, causes progressive enlargement of the central cavity. The sebaceous glands connected with each hair follicle remain practically normal. These hair follicle cysts become so large that if the skin is separated from the underlying tissue one can clearly distinguish by inspection with the naked eye numerous small white granules, which are visible through the subcutaneous tissue (figs. 1 and 2). The resemblance of these changes to those seen in ichthyosis follicularis (keratosis pilaris or lichen pilaris) is noteworthy.

It was felt that it would be of interest to determine the local action of estradiol on a skin in which keratinization and hair formation are seriously disturbed as a result of a genetic abnormality. Through the cooperation of the department of genetics, I obtained 8 postpubertal rhino mice, weighing 20 to 29 Gm. (average 26 Gm.) at the onset of the experiment. Four of these (1 male and 3 females) were treated with a solution of 250 micrograms of estradiol per cubic centimeter of peanut oil, which was rubbed into their backs by means of a cotton pad once

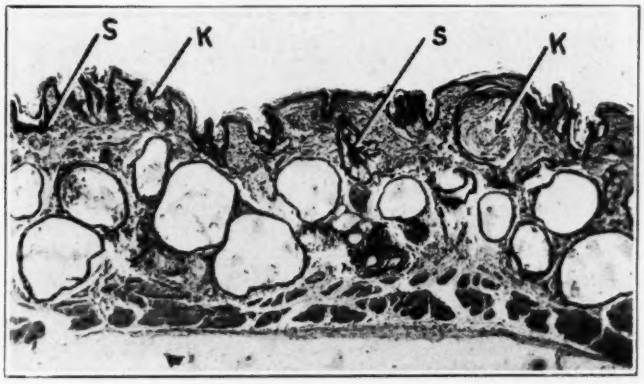

Fig. 2.—Section through the skin of a mouse in which the rhino type of skin was manifest. Note the absence of normal hair follicles. Follicles indicated by *K* are keratinized, the one on the right being the largest keratinized follicle in a series of sections through the skin of untreated rhino mice. The light cysts in the lower layers of the derma contained an amorphous material, perhaps partly sebaceous secretion, which was dissolved in the process of fixation, dehydration and embedding. The sebaceous glands, marked *S*, are well preserved.

daily for four months. The remaining 4 mice (2 males and 2 females) served as controls and were treated with pure peanut oil in the same manner as the animals of the experimental group.

Within a few weeks after the initiation of the treatment the skin of the estradiol-treated animals became covered with a comparatively thick layer of brownish, cornified epidermal scales, which readily sloughed off when the area was rubbed; after this the thickness of the derma increased slowly, but constantly, throughout the entire period of treatment. During the final stages the difference between the treated and the untreated animals could easily be recognized by taking up a fold of skin between two fingers.

At the end of the fourth month of treatment all the animals were killed and the skin was carefully dissected from the underlying tissue. With the naked eye it was easy to see that the fine white granules, which are readily visible through the subcutaneous tissue of rhino mice, were greatly enlarged in the estradiol-

treated animals, so that, viewed from the subcutaneous tissue side, the skin of the treated mice exhibited a coarse granular appearance (fig. 3).

On histologic examination the most outstanding change induced by estradiol proved to be an enormous increase in the production of keratin and its accumulation within the abnormal hair follicles. The sebaceous glands disappeared almost

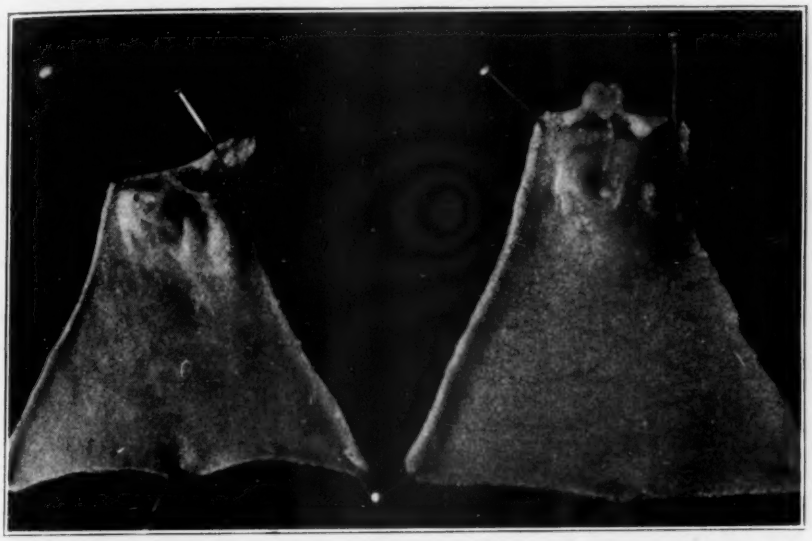

Fig. 3.—Macroscopic view of the caudal part of the skin of the back taken from an untreated and from an estradiol-treated rhino mouse. The dermal side of the skin is uppermost. Through the subcutaneous tissue one may readily distinguish the fine granules in the skin of the untreated mouse (left) and the coarse granules in that of the estradiol-treated mouse (right).

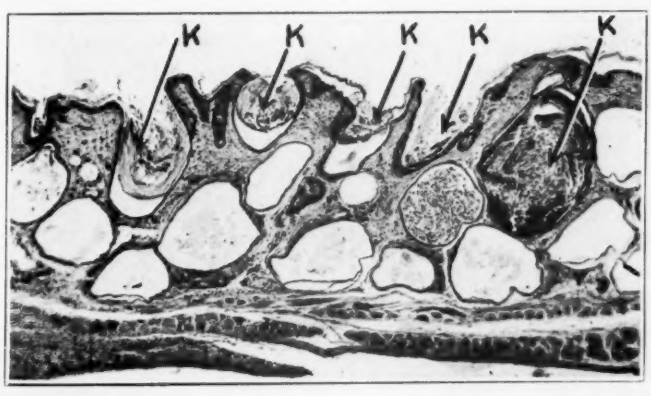

Fig. 4.—Section through the skin of a rhino mouse treated with estradiol. Note the large number of keratinized follicles, indicated by *K*. These follicles are greatly dilated with cornified squamous cells, and most of them are in the process of discharging their contents onto the surface of the skin. Sebaceous glands have entirely disappeared.

completely, perhaps as a result of pressure from the cysts. The surface epithelium was not significantly thickened, although it was perhaps somewhat more stratified than in untreated controls. The blood vessels of the corium were greatly dilated in all estradiol-treated animals. From these histologic observations it appears that

the thickening of the skin in the estradiol-treated mice was mainly due to the fact that under the influence of this substance the hair follicles produced an abnormally great amount of keratinized material, which distended the follicular cavities and thus increased the thickness and the granular appearance of the skin. Since many of these follicles discharge their cornified cells onto the free surface of the skin, the presence of the abundant scaly material could also be explained (figs. 1, 2 and 4). It should be emphasized that in spite of the local application of large quantities of estradiol to the naked skin of these animals, malignant changes have not been induced during the period of observation.

SUMMARY

The main histologic characteristics of the cutaneous structure of the rhino mouse are described, and their resemblance to the changes in ichthyosis follicularis is emphasized.

Chronic treatment by local application of estradiol to the skin of such animals caused increased keratinization of the abnormal hair follicles, hyperemia of the skin and involution of the cutaneous sebaceous glands. Malignant transformation of the congenitally abnormal skin was not observed during the four month period of observation.

The expenses of this investigation have been defrayed through a grant in aid from the International Cancer Research Foundation. Dr. A. G. Steinberg, of McGill University, donated the rhino mice, and Dr. Erwin Schwenk, of the Schering Corporation of Bloomfield, N. J., supplied the estradiol necessary for these experiments.

McGill University Faculty of Medicine.

PETROLEUM DERMATITIS

REPORT OF TWO CASES

MICHAEL G. ROSENBAUM, M.D.
HAIFA, PALESTINE

Persons whose professional work brings them in constant contact with petroleum suffer from dermatoses which do not differ essentially from those of paraffin workers who acquire the so-called vaselinoderma (Oppenheim [1]). Petroleum also produces erythematopapular, as well as papulopustular, itching eruptions of the hands, forearms and thighs, the favorite localities of most occupational dermatoses. In the follicles of the involved parts, especially on the dorsa of the fingers, small hard kernels of horn, similar to the lesions of keratosis follicularis, are formed, or in cases of secondary infection a follicular acne develops. The effect is totally different if petroleum comes in contact (even on a single occasion) with the sensitive normally covered areas of the skin. On rare occasions there is bullous dermatitis. A search of the literature brought to light only the following reports of contact dermatitis due to petroleum:

1. In 1929, Fellner [2] reported a case of petroleum dermatitis in a 54 year old woman who had treated her sore throat by applying a petroleum-soaked compress. Bullous dermatitis developed, which spread over most of the trunk and the proximal half of the thighs. She died five days later.

2. In 1935, Adams and Irby [3] published the first case in detail. The patient was a petroleum worker in whom vesiculobullous dermatitis of the hands, arms, feet and legs developed after these areas had been soaked with fluid from an oil well. The authors saw the man two days after the exposure to oil. The eruption became rapidly worse during the next few days, so that the patient had to be sent to a hospital. He recovered within a fortnight. The fluid in the unbroken vesicles was thin and milky. The authors called special attention to the rarity of the eruption and to the fact that in a large refinery no cases had been previously encountered for fourteen years.

3. Three Netherland authors, Beek,[4] Dwarshuis [5] and van Kekem,[6] reported 3 more cases in 1937. In Beek's case, that of a 3 year old boy, the dermatitis developed after contact with petroleum-soaked clothes. Dwarshuis said that in his case the same condition developed from contact with dilute petroleum for thirty-six

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From the Section of Dermatology, House Elfenbein, service of Dr. Michael G. Rosenbaum, assisted by the workers' sick fund, Kupat Chelim.

1. Oppenheim, M.: Ueber eine durch unreines Vaselin als Salbengrundlage verursachte Hauterkrankung, Wien. klin. Wchnschr. **29**:1293, 1916; Vaselenederma verrucosum, Arch. f. Dermat. u. Syph. **131**:272, 1921.

2. Fellner, abstracted, Dermat. Wchnschr. **89**:1375, 1929.

3. Adams, J. M., and Irby, F. L.: Contact Dermatitis Due to Crude Petroleum, Arch. Dermat. & Syph. **32**:573 (Oct.) 1935.

4. Beek, C. H.: Dermatitis Bullosa Caused by Petroleum, Nederl. tijdschr. v. geneesk. **81**:472, 1937; abstracted, Dermat. Wchnschr. **105**:967, 1937.

5. Dwarshuis, P. C.: Case of Dermatitis Bullosa Caused by Petroleum, Nederl. tijdschr. v. geneesk. **81**:1325, 1937; abstracted, Dermat. Wchnschr. **105**:1626, 1937.

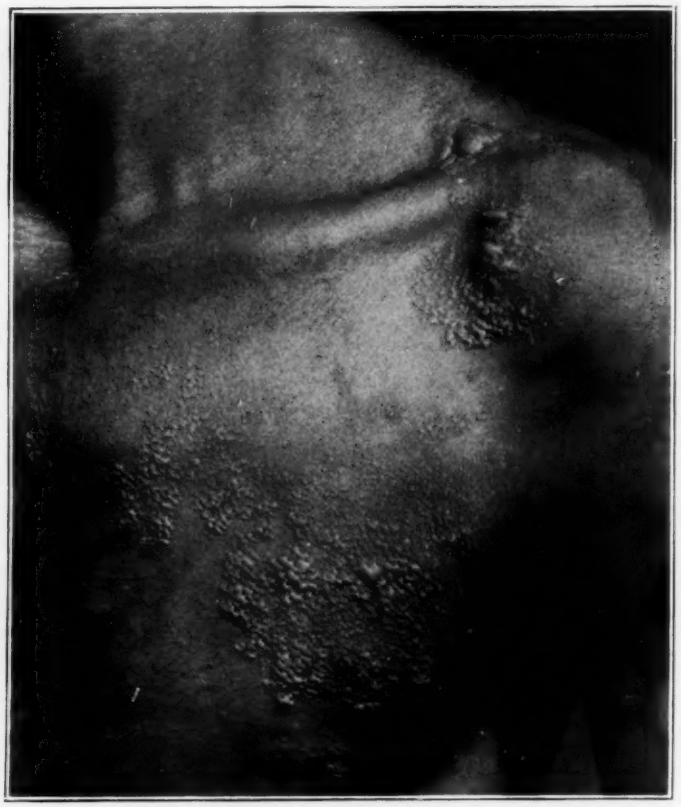
6. van Kekem, A. J.: Case of Dermatitis Bullosa Caused by Petroleum, Nederl. tijdschr. v. geneesk. **81**:2515, 1937; abstracted, Dermat. Wchnschr. **105**:1626, 1937.

hours. In the case of van Kekem the eruption appeared after contact for five to ten minutes with petroleum-soaked clothes.

Considering the rarity of the publications, the report of the following 2 cases seems justified.

REPORT OF CASES

CASE 1.—M. K., a 48 year old man, a worker in a glass factory, stated that on the previous day he had been assigned to the department of glass cutting. His work there was as follows: He first rubbed the glass plate with petroleum and then held it with the edge against his abdomen, so that petroleum continually soaked his overalls, as he cut the glass with a diamond. On the evening of the same day he noticed itching, and later a burning pain, in the skin of his abdomen. Examination showed a round superficial blister in the right lower



Petroleum dermatitis.

abdominal quadrant, against which the glass plates had been held. The blister was 8 cm. in diameter, and the roof was torn. Underneath was a superficial ulcer, with a dull red, non-bleeding base. It was assumed that the blister was subcorneal. Surrounding it was a bright red, edematous zone of inflammation of a hand's breadth. There were no enlarged lymphatic glands. The patient was well developed and well nourished and did not appear ill. The diagnosis was acute bullous dermatitis due to contact with petroleum.

CASE 2.—J. B., a youth aged 19 years, went to bed without any signs of an eruption on the evening of Sept. 14, 1942. The bed and straw mattress had been disinfected with petroleum the same day. The sheet was fresh and had not been disinfected. The next morning he awoke with rather violent itching on the left side of his chest, the side on which he was accustomed to sleep. He noticed a curious rash, which he showed to me four hours later.

Examination revealed inflammation on the left side of the chest, which extended from the supraclavicular region down almost to the nipples. There were hundreds of canary yellow vesicles, which contrasted with the bright red background. The blisters varied from the size of a pinhead to that of a plum and were mostly grouped. On the shoulder they were fewer. They were strikingly flaccid, so that the tops wrinkled when touched. The bullae above the left clavicle apparently originated from the confluence of several vesicles. Under the microscope, the thin, seropurulent contents of the lesions showed compact sterile clusters of leukocytes, but no bacteria. The regional lymphatic glands were enlarged. The patient was in good general health, with normal temperature.

COMMENT

There was no doubt about the diagnosis. In both cases there was a typical picture of acute dermatitis due to the external influence of a chemical agent. I saw both patients within a few hours after the appearance of the eruption and within a day after exposure to the sensitizing agent. The statements of the 2 patients were clear and exact, and there was no reason to doubt their accuracy. I should like to mention the following characteristics of the clinical picture:

1. The canary yellow color of the blisters. The color, which was due to the sudden invasion of leukocytes into the upper layers of the epidermis within a few hours, was especially striking. According to one of the patients (case 2), the blisters had the same yellow color early in the morning, a purely serous stage not having been observed.

2. The extraordinary flaccidity of the unbroken vesicles. The flaccidity might be explained by the fact that on the sudden separation of the stratum corneum from the stratum malpighii the texture of the two strata had also been loosened in the surrounding area. When the contents of the blisters sank, under the influence of gravity, and found their way between the two layers, the blister became too large for its contents.

3. The bright red, inflammatory areola surrounding the bullae and vesicles.

I wish to emphasize these three characteristics of the clinical picture, because Adams and Irby [3] mentioned only the milky color of the blisters. Nothing more can be said about the subsequent course of the eruption, as both patients failed to return after the first consultation. It is probable that the eruption healed quickly and that the height of the process occurred on the first day after exposure to the irritant. Adams and Irby [3] said that in their case the eruption became worse on the third day and that the patient had to be hospitalized. The great rarity of this disease, as shown by the few publications, is striking. This is especially surprising in a land where there is a large oil industry and where petroleum is generally used in such housekeeping activities as cooking and sweeping the floors.

I think that mechanical friction from the heavy glass plates against the abdomen and the petroleum produced the dermatitis in case 1. In case 2 the extension of the dermatitis corresponded to the cutaneous surface on which the patient lay on his sheet. The night was hot, and the patient perspired. The wet sheet absorbed some of the petroleum poured over the straw mattress. A small quantity of petroleum in contact with the wet skin for several hours was sufficient to cause the bullous dermatitis. The patient's legs, which did not perspire, did not become inflamed. The effect of perspiration should not be underestimated in a subtropical climate. In Palestine, particularly in the summer months, artificial dermatoses easily become vesicular or bullous. Adams and Irby [3] also expressed the opinion that contact dermatitis due to petroleum develops only if the skin is wet.

SUMMARY

Two cases of bullous dermatitis due to a single contact of a few hours with petroleum are presented. Cases of this type are apparently uncommon, as few reports have appeared in the literature. This rarity is due to the fact that the presence of three factors is necessary for the development of petroleum dermatitis: (1) the action of petroleum, (2) individual susceptibility and (3) intense perspiration, friction or other mechanical irritation of the skin.

The clinical picture of this disease is characterized by (1) canary yellow blisters, (2) extraordinary flaccidity of the unbroken vesicles and (3) a red, edematous zone around the blisters.

House Elfenbein.

Clinical Notes

DERMATITIS DUE TO NAIL POLISH FOUNDATION

LIEUTENANT JOSEPH M. SHELTON (MC), U.S.N.R.

Dermatitis due to nail polish has been described frequently during the past two years. The case I am reporting demonstrates that nail polish is not the only nail preparation that may be at fault.

REPORT OF A CASE

Mrs. R. G., a white woman aged 28, consulted me on Aug. 4, 1942 because of an eruption involving her eyelids and cheeks of four months' duration. Examination showed a typical contact dermatitis of the upper eyelids and cheeks at the angles of the mouth. It had undergone numerous exacerbations at irregular intervals. She had been using her present brand of nail polish for several years and had changed the shade three months previously. The history was irrelevant regarding the use of perfume, wave set fluid and other significant preparations. Patch tests were performed with the patient's brand of nail polish and with two other brands, including a clear lacquer. The reactions were all negative at the end of forty-eight hours. However, the patient stated that on returning home she realized that she had not mentioned her use of nail polish foundation, a preparation used prior to the application of polish. She immediately applied a small quantity of this liquid to a circular area on her left forearm. At the time the patch test was read a circular area of vesicular dermatitis was present at that site. When the patient was questioned further it was discovered that the eruption and its subsequent exacerbations closely coincided with the use of the polish foundation. This preparation is a colorless liquid of the same consistency and drying time as ordinary nail lacquer.[1]

Subsequent patch tests were made with (1) the patient's nail polish, (2) nail polish foundation, (3) a layer of foundation which was allowed to dry completely and then overlaid with a coat of nail polish and (4) clear nail polish. It was necessary for the patient to remove the test material in thirty-six hours because of a severe vesicular reaction to both the foundation and the combination of foundation and polish. Both reactions were graded as 4 plus. The reactions to the other substances were negative. It was noted at the time of application that the foundation and the nail polish were miscible and were mutual solvents. It seems likely that polish applied over a dry layer of the foundation readily absorbs sufficient of the latter to become a sensitizer.

COMMENT

I feel that this case is of interest since it demonstrates that other finger nail preparations can produce the same pattern of dermatitis as that which may be caused by finger nail polish.

6 South Main Street.

From the Pittsburgh Skin and Cancer Foundation.

1. A communication from the manufacturer states that the polish and the foundation "are similar in composition, being composed of nitrocellulose dissolved in the customary solvents used for that purpose, such as butyl acetate, ethyl acetate, alcohol, etc. The nail polish is of course colored with certified dyes, while the foundation is a colorless lacquer combined with a minute quantity of wax dispersed to give the slightly turbid, silvery effect required."

ADENOMA SEBACEUM TREATED BY SOLID CARBON DIOXIDE

THEODORE H. FINKLE, M.D., FAR ROCKAWAY, N. Y.

More or less satisfactory results have been obtained in cases of adenoma sebaceum with various therapeutic methods, such as electrolysis, electrodesiccation, cautery and ultraviolet irradiation.

Fig. 1.—Adenoma sebaceum of the forehead, nose, cheeks and chin.

The case reported herein demonstrates the ease and efficiency with which small or moderate-sized lesions of adenoma sebaceum may be eradicated by solid carbon dioxide.

REPORT OF A CASE

R. H., a Jewess aged 30, entered the clinic for treatment of lesions on her toes.

Examination showed numerous shiny flesh-colored to erythematous papules 1 to 4 mm. in diameter on the forehead, nose, cheeks and chin. Telangiectasia was observed among the lesions. On some of the toes were nontender, smooth flesh-colored nodules ranging from 3 to 8 mm. in diameter. These nodules were attached to the nail folds of the first and third toes of the right foot and the first, second and third toes of the left foot.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

The patient gave a history of having had the lesions on the face and toes since childhood. She had two children, one of whom was retarded mentally.

The results of laboratory examinations were as follows: The basal metabolic rate was normal. The Wassermann reaction of the blood was negative. The results of complete studies of the blood and urinalysis were found to be within normal limits. Neurologic and psychiatric examinations, including electroencephalographic studies, were made in the New York Post-Graduate Medical School and Hospital and showed no significant changes from the normal. The patient refused to allow a biopsy.

Peeling treatment of the facial lesions with solid carbon dioxide was attempted. The solid carbon dioxide was shaped in the form of a pencil and applied in a rotary manner until

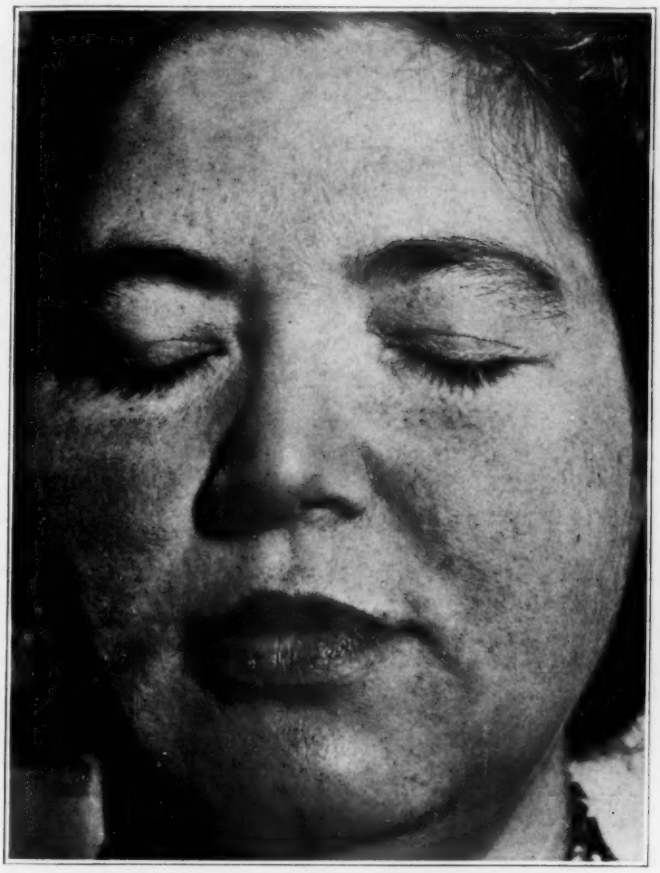


Fig. 2.—Results of five treatments with solid carbon dioxide.

blanching was obtained. Eight to fifteen seconds in any one area under moderate pressure was sufficient to produce the desired effect. The pencil of solid carbon dioxide was kept moving over the skin at all times from one small area to another until the entire affected area was treated. For the edema, erythema and pruritus which followed the treatment, wet dressings of boric acid solution and soothing ointments were used.

After the patient received five treatments at ten to fourteen day intervals there was definite improvement, as shown in the accompanying illustrations.

1300 Cornaga Avenue.

Correspondence

A PLAINT, A PLEA AND A PROPOSAL

To the Editor:—This letter has been in nascent form for some time. During the past several years it received frequent stimuli from various sources which animated its rate of development. Ultimately it was precipitated by an article in a recent issue of one of the weekly medical journals on the use of coal tar in the treatment of cutaneous diseases. The article in question is a well written discussion touching briefly on the historical background and the pharmacy and pharmacology of crude coal tar. In it are also listed ten dermatoses, covering an extensive field, for treatment of which the value of coal tar is discussed. However, the essential intent of the article is obviously to advocate and endorse an ointment of coal tar manufactured by a pharmaceutical company under a so-called "trade name." This particular preparation is not listed as accepted by the Council on Pharmacy and Chemistry of the American Medical Association in the latest edition of "New and Nonofficial Remedies" or its supplement.

It so happened that only a few days after this article was published, an advertisement vigorously and profusely extolling this preparation was received by mail from the manufacturer. The subject of the plaint lies partly in the very fact that a dermatologist of the author's eminence recommends to the general medical reader a ready-made ointment of the type commonly referred to as "proprietary," regardless of how acceptable to another dermatologist may be his rationale for employment of this particular preparation. It is the principle which is reproved.

In the environs of Boston there are obtainable at least two other coal tar ointments of a "proprietary" character, each of which has been advocated by various dermatologists in literature for the medical reader; neither preparation is "accepted." In a recent issue of one of the widely read, small-sized, gratuitously distributed publications facetiously referred to as "throw away magazines," in a total content of 150 pages there were fourteen advertisements for "proprietary" dermatologic preparations; nine were full page! One preparation is advertised as able to "stop this . . . insidious saboteur" (referring to industrial dermatoses) and as "composed of liquor carbonis detergens, lanolin, U. S. P. and menthol, U. S. P. in a special cream base." The manufacturer of another tar preparation cites "the clinical findings" of the author of a book on cutaneous diseases. One is advertised as a "speedy—easy—efficient treatment for fungous infections." Not one is accepted by the Council on Pharmacy and Chemistry! Even the most recent publication on dermatology by the National Research Council mentions at least two of these proprietary mixtures and thus gives them a half-hearted sort of an ethical standing, to which they are not really entitled. These examples can be multiplied many times.

The objections to these mixtures are so self evident that it should be superfluous to point out, for instance, that the potent ingredients are fixed in amount and are therefore only occasionally proper for use in a particular case. It should not be necessary to indicate that by remembering only a "catchy trade name" one quickly forgets the actual formula and is soon in the rut of prescribing by rote. Certainly it should be evident that soon after a reputable dermatologist endorses one of the "patent medicines," no matter how high the initial ethical standards of the manufacturer, it will be found in the drug store windows and on the department store shelves for the self medication of the public.

The plea is for a more active interest in and support of the machinery already existing for the maintenance of high standards of therapy, namely, the Pharmacopeia of the United States, the National Formulary, and the New and Nonofficial Remedies of the Council on Pharmacy and Chemistry of the American Medical Association. It is highly worth while for every teacher of dermatology to be acquainted with the "official rules" of the Council. Arguments for these three great agencies are superfluous here. It may even be redundant to point out that in the seventh edition of the National Formulary there are, among others, the following items of special interest to dermatologists: two liniments, twelve solutions, six lotions, one magma, eight pastes and thirteen ointments. Of coal tar, there are three preparations: a solution, a chloroformic solution and an ointment.

These three standard publications should be the principal source of information regarding pharmaceutic combinations which are already compounded and of whose strength, purity and method of preparation there is a dependable regulation. It would be ideal for each dermatologist to have a pharmacy connected with his office. In no other branch of medicine does so much depend on the art and technic of the pharmacist. When the general practitioner

refers a problem to a dermatologist he has every reason to expect the specialist to be armed with an adequate pharmacologic armamentarium, so that the patient will receive the prescriptions best devised to fit all conditions peculiar to that particular person at that particular time; only infrequently, if at all, should he expect from his consultant some prefabricated semiscientific mixture of which he has received in that morning's mail a gratuitous unasked-for sample.

The proposal is therefore that more interest in the pharmacy and pharmacology of dermatology be fostered in a more concerted manner. There should be an active standing committee to receive recommendations and publish reports and generally act as a clearing house for all such matters. Perhaps it can be sponsored by some one or all of the important organizations of dermatologists, such as the American Academy of Dermatology and Syphilology, the Section on Dermatology and Syphilology of the American Medical Association, the American Dermatological Association and the sectional societies. When progress demands a certain form of medication, such as a special standardization of coal tar or a water-miscible ointment base, this committee, made up of dermatologists, would be the most logical one to initiate the most efficient action resulting in an official preparation. Problems relating to the teaching of students of pharmacy, the compounding by druggists and even general principles of relations between druggists and doctors in respect to dermatologic pharmacy could be handled by this committee acting as a liaison organization between the dermatologists and the American Pharmaceutical Association.

True, dermatology is represented on the committees which revise these three standard books. But this is not enough. There should be continuous interest in these problems in a cooperative, effective plan which would encourage more general participation in the maintenance of high standards of dermatologic pharmacy. In attempting to avoid the Charybdis of the occasional ineptitude of the local druggist one must not crash into the Scylla of the use of unrecognizable proprietary preparations.

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News and Comment

SECOND ANNUAL MEETING OF CONSULTING STAFF OF DERMATOSES INVESTIGATIONS SECTION

At the meeting of the Consulting Staff of the Dermatoses Investigations Section at Bethesda, Md., on June 14 and 15, 1943, four members met with Dr. Louis Schwartz and his staff, including Drs. Paul A. O'Leary (chairman), W. William Becker, Howard Fox and Harry J. Templeton. Captain Richard L. Sutton Jr., Medical Corps, Army of the United States, resigned after entrance into the armed forces. Dr. Samuel M. Peck was present as a commissioned officer of the United States Public Health Service.

The first course in occupational dermatoses was given July 27 to Aug. 8, 1942, at the National Institute of Health, Bethesda, Md. At the first meeting it had been decided that persons to participate in the course should be selected with the help of the consulting staff. Since there was not a sufficient number of applicants, individual selection was not necessary. The course was repeated in Chicago, Jan. 11 to 23, 1943, under the auspices of the American Medical Association. A much larger group participated.

It was decided that a similar course should be given later this year, probably in the fall, and again in the early part of next year, as conditions warrant. It was suggested further that two types of courses might be given: one for industrial physicians and dermatologists, which would be conducted in a similar manner to those previously given, and another which would consist of a correspondence course.

It was tentatively decided that one of the courses should be given in a large industrial center in the East, such as New York, and the other in the Middle West in a city centrally located, such as St. Louis

The participation of the consulting staff in the course was discussed. It was suggested that members of the consulting staff living in the vicinity of the cities where the course is to be given should speak on a subject related to industrial dermatoses in which they are particularly interested.

The publications and research activities of the Dermatoses Investigations Section since the last meeting were reviewed. There has been developed a protective ointment against tetryl which is also efficacious against poison ivy.

Dr. Mason discussed his investigations of the active dermatitis-producing principles of poison ivy. Several active principles have been successfully isolated.

Dr. Peck discussed the investigations which he has been conducting in association with Dr. Botvinick on dermatophytosis, including the possibilities of infection with dermatophytosis from flooring, especially in shower rooms and similar places. In collaboration with Dr. Mason the active principles of trichophytin are also being studied. The question of whether workers with fungous infections and a sensitivity to fungi and their products are especially susceptible to contact allergic dermatitis is a special point in these investigations.

Dr. Schwartz was able to report that no trouble has been reported from the use of patch tests as a diagnostic measure.

Dr. Dunn described the patch tests which he had been carrying on in testing materials for the Army and Navy. With these tests he has been able to rule out a number of primary irritants.

A review of some of the work of the Dermatoses Section on the development of ointments as protectives against war gases was given. Dr. Schwartz announced that apparently an efficacious ointment has been developed against mustard gas and lewisite.

This section is carrying on investigations with the view to develop indicator soaps, that is soaps which will change color in the presence of substances such as tetryl, TNT and fulminate of mercury.

Dr. Gant reported on the experiments being carried on with insect repellents.

Dr. Goldsmith carried out thorough experiments in a number of ordnance plants with the tetryl-protective cream developed in this section. Results of the study indicated that only 25 per cent of the workers who were sensitive to tetryl were protected by the use of the cream.

Dr. Peck discussed the dermatitis from carrots which he recently investigated. Results of these studies will soon be submitted for publication.

Another compilation of the abstracts of the world literature on industrial dermatoses is practically complete and will soon be published.

A tentative program for the work of the coming year was outlined. It was the opinion of the consultant staff that the work already started should be continued.

The consultant staff agreed that the work of the section was most laudable, and they felt that the time devoted to this meeting was worth while. A vote of thanks was given to Dr. Schwartz and his staff for the kindness shown them during their visit.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

CEREBRAL REACTIONS ASSOCIATED WITH MASSIVE MAPHARSEN TREATMENT OF EARLY SYPHILIS. E. W. THOMAS, G. WEXLER and B. DATTNER, Am. J. Syph., Gonor. & Ven. Dis. **26**:529 (Sept.) 1942.

Seven hundred and sixty-four patients with early syphilis were treated with massive dosages of mapharsen by the syringe injection method. Eight patients had symptomatic cerebral reactions, 2 of whom died. An additional 8 patients had no definite symptoms, and the diagnosis was made only by means of examination of the spinal fluid. No deleterious sequelae have been observed in any of those who survived. Reactions of the cerebrospinal axis following arsenical drugs vary as to time of onset in relation to treatment and as to duration of symptoms.

The authors believe that the cerebral reactions are vascular and that the functional damage to cells is out of proportion to the structural changes found. Whether syphilis itself accounts for the reactions in some of the cases observed by the authors remains undetermined.

No means of anticipating arsenical encephalitis has been found. The criteria for interrupting massive dosage with mapharsen in the absence of definite clinical signs of encephalitis are the finding of cells and increased protein, especially the latter, in the spinal fluid.

THE IMPORTANCE OF THE TIME FACTOR IN THE EVALUATION OF "CURE" IN SYPHILITIC RABBITS. H. EAGLE, R. B. HOGAN and J. E. KEMP, Am. J. Syph., Gonor. & Ven. Dis. **26**:557 (Sept.) 1942.

The result of a lymph node transfer to a normal rabbit has been the ultimate criterion of cure in experimental rabbit syphilis.

Apparently "cured" rabbits, as judged by negative lymph node transfers into normal rabbits six weeks after treatment, were retested by a second node transfer some six months after treatment, and 37 per cent were found to have become infectious in the interim.

Existing data as to the therapeutic efficacy of various arsenicals must be reconsidered in the light of this finding.

INTRAVENOUS THIAMIN CHLORIDE (VITAMIN B_1) IN THE TREATMENT OF TABETIC LIGHTNING PAINS. K. D. COCHEMS and J. E. KEMP, Am. J. Syph., Gonor. & Ven. Dis. **26**:574 (Sept.) 1942.

The intravenous administration of thiamine hydrochloride is valueless for the alleviation of tabetic lightning pains in a majority of cases and is of doubtful value in the remainder. Further clinical trial with thiamine, possibly by other routes of administration or in conjunction with other vitamins, is necessary before final opinion is permissible.

THE SENSITIVITY AND SPECIFICITY OF THE KAHN REACTION IN THE TEMPERATURE RANGE FROM 37° C. THROUGH 56° C. WITH SYPHILITIC SERA: WITH A CONSIDERATION OF THE VALUE OF THE KAHN VERIFICATION TEST IN SYPHILIS. M. N. GREEN and G. F. FORSTER, Am. J. Syph., Gonor. & Ven. Dis. **26**:632 (Sept.) 1942.

Kahn verification tests employing reaction temperatures above 37 C. show that in the majority of syphilitic serums maximum sensitivity without loss of specificity occurs at approximately 45 C., dropping off slightly but progressively at 50 and 56 C. The possible importance of this fact in the laboratory diagnosis of syphilis is pointed out. It appears that the usefulness of the verification reaction lies in the diagnosis of syphilis no less than in the recognition of false positive reactions.

PRELIMINARY INTENSIVE TREATMENT OF PRIMARY SYPHILIS BY DAILY INJECTION OF ARSENICALS. I. A. PELZMAN and E. GREENWALD, Am. J. Syph., Gonor. & Ven. Dis. **26**:637 (Sept.) 1942.

The authors, members of the Medical Corps of the United States Army, have treated 105 patients with primary syphilis by daily injections of an arsenical drug. This scheme of treatment has reduced the number of noneffective days (days of hospital confinement) by 42 per cent (nine and three-tenths to five and four-tenths days).

Neoarsphenamine in daily repeated doses of 0.45 Gm. produced a high incidence of complications. Mapharsen may be used in daily doses of 0.06 Gm. for five days effectively to reduce hospital days, without risk of serious complications.

After this intensive preliminary treatment, each patient was given the usual course of treatment for primary syphilis as recommended by the Cooperative Clinic Group.

REUTER, Milwaukee.

PURPURA ANNULARIS TELANGIECTODES (MAJOCCHI) AND PROGRESSIVE PIGMENTARY DERMATOSIS (SCHAMBERG). FRED WISE, J. Invest. Dermat. **5**:153 (Aug.) 1942.

The author differentiates between Schamberg's progressive pigmentary dermatosis and purpura annularis telangiectodes (Majocchi's disease) clinically and pathologically. The chief bond of relationship between the two dermatoses is their dependence on impairment of the capillaries of the skin with a concurrent arrangement of circulation. In Schamberg's disease the dominant clinical feature consists of hyperpigmented, reddish brown to dark brown patches of skin with peripheral zones of cayenne-pepper-like puncta. The patches may be single or multiple; they usually are situated on the lower third of the leg and are most often encountered in adolescent and adult males. The onset of the eruption is insidious, and it may progress for many months or years. Relapses and abrupt exacerbations do not occur. There is an absence of telangiectases and of annular formations. The chief histologic changes consist of an exudative inflammatory process which is most pronounced in the upper zones of the cutis, perivascular focal and diffuse cellular infiltrations, diapedesis of the red blood cells and deposits of hemosiderotic granules. There is absence of telangiectases, aneurysmal sacculation and hyaline degeneration of the vessel walls.

In purpura annularis telangiectodes the dominant clinical feature consists of telangiectases and punctate lesions resembling petechiae. In the classic eruption vascular annular lesions are conspicuous. Hyperpigmentation is a later manifestation. The sites of predilection are the lower extremities, but any part of the body may be involved. Spontaneous regression, remissions and exacerbations have been recorded. The eruption occurs in the young and old of both sexes and may be associated with serious impairment of the patient's health. Histologically the eruption is characterized by engorgement and dilatation of the small vessels, by numerous telangiectatic vessels accompanied by deposits of blood pigment and by perivascular small cell infiltration. In later stages, the blood vessels undergo an obliterating endoarteritis; aneurysmal sacculation and hyaline degeneration of the vascular walls are frequently observed.

EXPERIMENTALLY INDUCED DISAPPEARANCE AND RE-APPEARANCE OF LESIONS OF HYDROCYSTOMA. A. DOSTROVSKY and F. SAGHER, J. Invest. Dermat. **5**:167 (Aug.) 1942.

The authors were able to cause the disappearance of the vesicles of hidrocystoma by the oral administration of atropine sulfate in the course of three to seven days. By administration of pilocarpine hydrochloride the cysts could be made to reappear after two to ten days. It seemed apparent to the authors that the experimental and spontaneous appearance and disappearance of the cysts took place only in glands with a particular predisposition which was inherent in the ducts of individual sweat glands.

PULMONARY FAT EMBOLISM FOLLOWING INFUSIONS VIA THE BONE MARROW. U. J. WILE and IRA L. SCHAMBERG, J. Invest. Dermat. **5**:173 (Aug.) 1942.

The authors attempted the introduction of the massive arsenotherapy of syphilis by the drip method via the bone marrow. Nine adult male rabbits were used, and the tibia, femur and humerus were the bones selected for injection. Light anesthesia was maintained during the entire course of each treatment by repeated intraperitoneal injections of sodium pentobarbital. The daily dose of mapharsen was 4 mg. per kilogram of body weight in a dilution of 1 mg. of mapharsen in 10 cc. of 5 per cent dextrose solution. Seven rabbits were given five successive daily bone marrow infusions and were killed from the fifth to the nineteenth day of the experiment. Two control animals, which received five daily intravenous infusions, the dosage and dilution of the drug and the experimental conditions, including anesthesia, being identical with those used in the test group, were killed on the tenth and sixteenth days. The most striking pathologic observation was fat embolism in the pulmonary arterioles, which was seen in 5 of the 7 rabbits treated by the bone marrow route; no fat emboli were seen in the 2 animals treated by vein. In 1 rabbit, fat embolism was the cause of sudden death at the termination of the fifth treatment. Special stains showed large fat globules, in most cases surrounded by foreign body giant cells, filling the pulmonary arterioles.

The authors conclude, in view of the finding of pulmonary fat embolism in animals treated by bone marrow infusion, that this procedure cannot at present be considered free from hazard in human beings.

TOBACCO SKIN-REACTIONS IN PERIPHERAL VASCULAR DISEASES AND CORONARY ARTERY DISEASE. MAYER A. GREEN, J. Invest. Dermat. **5**:179 (Aug.) 1942.

The author noted the occurrence of approximately seven times as many positive cutaneous reactions to tobacco only in patients with thromboangiitis obliterans with no history of allergy as in the normal population. This indicates that these reactions are not merely another manifestation of the polyvalent sensitivity of the skin generally characteristic of atopic persons but a specific cutaneous sensitivity, resulting from repeated absorption of this allergen. The finding of 42 per cent of positive reactions to tobacco only in smokers with peripheral vascular disease over 45 years of age, a ratio of 4 to 1, as compared with observations in the general population suggests that tobacco hypersensitiveness may contribute to the symptoms of intermittent claudication, etc., seen in these older persons.

STUDIES IN ABNORMAL HUMAN SENSITIVITY TO LIGHT: I. PRURIGO AESTIVALIS, ECZEMA SOLARE AND URTICARIA PHOTOGENICA; REPORT OF 17 CASES AND REVIEW OF THE LITERATURE; II. LIGHT SENSITIVITY IN PRURIGO AESTIVALIS, ECZEMA SOLARE AND URTICARIA PHOTOGENICA; REPORT OF EXPERIMENTS. STEPHAN EPSTEIN, J. Invest. Dermat. **5**:187 (Aug.); 225 (Oct.) 1942.

The author discusses a group of diseases, consisting of urticaria photogenica, eczema solare, prurigo aestivalis and their combinations, in which three different types of sensitivity to light were demonstrated: (1) immediate urticarial (whealing) reaction, (2) pathologic sunburn-like reaction and (3) provocation of specific lesions of prurigo. These three manifestations of hypersensitivity to light seem independent of each other; they correspond essentially to the clinical entities of urticaria photogenica, eczema solare and prurigo aestivalis. In diseases which clinically represent combinations of the different types, more than one form, and even all three forms, of light sensitivity have been found, which explains the variety of clinical manifestations. The results of the light tests need not parallel at all times the clinical manifestation of a patient suffering from multiple forms of light sensitivity. The three forms of light sensitivity are not due to specific wavelengths. Every one of them has been provoked by more than one spectral region.

DERMATOPATHIC LYMPHADENITIS: FOCAL GRANULOMATOUS LYMPHADENITIS ASSOCIATED WITH CHRONIC GENERALIZED SKIN DISORDERS. ELLIOTT HURWITT, J. Invest. Dermat. **5**:197 (Aug.) 1942.

The author calls attention to the occurrence of generalized lymphadenopathy in association with a variety of chronic disease of the skin characterized by pruritus. He stresses the fact that the histologic features of the lymph nodes point to a benign reactive process. Clinically, the majority of the cases reported were supposed to be instances either of an intrinsic lymph node disease, such as Hodgkin's disease or lymphosarcoma with cutaneous involvement, or of mycosis fungoides with secondary lymph node infiltration.

RELATIONSHIP BETWEEN CERTAIN PHYSICO-CHEMICAL CHANGES IN THE CORNIFIED LAYER AND THE ENDOGENOUS BACTERIAL FLORA OF THE SKIN. LLOYD ARNOLD, J. Invest. Dermat. **5**:207 (Oct.) 1942.

The exogenous bacterial flora residing on the surface of the skin can be increased by alkalinization and by exposure to warm weather and to warm humid air. The same flora can be decreased by exposure of the skin to acid. The cornified layer behaves like a colloidal gel structure; increase in water content causes an increase in the surface endogenous flora. Dehydration of this layer is associated with a decrease in the viable bacteria on the surface. The flora returns to the normal density when the cornified layer readjusts itself. This requires about half an hour after alkalinization and two hours after acidification. The survival of exogenous bacteria follows the same pattern. A cornified layer with increased water content permits exogenous bacteria to survive for longer periods of time; a dehydrated layer rapidly renders bacteria nonviable.

THE REMOVAL OF DIVALENT CATIONS FROM SOLUTION BY BEEF HEART ANTIGENS. L. F. PIERCE and EDWARD L. BREAZEALE, J. Invest. Dermat. **5**:249 (Oct.) 1942.

The authors advance a new theory of the mechanism of syphilitic serologic reactions. Calcium and magnesium were removed from aqueous solutions by means of Kahn and Hinton

antigens. Calcium and magnesium were removed from solution by Kahn antigen and the floc removed by filtration. The floc was then washed with saline solution, and the calcium and magnesium recovered in the filtrate. It appears that the production of a floc depends on the degree of ionization of calcium and not merely on its molecular availability. That is to say, there must be either an increase in ionization of divalent cations or some profound vectorial shift with respect to the ionization constant of calcium compounds in seropositive serums which causes the antigen to form a floc. Beef heart antigens are acting purely in the capacity of a zeolite and shift from a sodium salt to either a calcium and/or magnesium salt, thereby producing a floc.

EXPERIMENTAL CUTANEOUS REACTIONS OF AMERICAN BLASTOMYCOSIS IN THE GUINEA PIG. LAWRENCE M. NELSON, J. Invest. Dermat. **5**:257 (Oct.) 1942.

The author concludes from his experiments that in guinea pigs experimentally infected with Blastomyces dermatitidis a specific allergic reaction to the organism develops. This allergic reaction may be demonstrated by a tuberculin-like reaction forty-eight hours after intracutaneous injection of killed dermatitidis organisms, the broth in which they grew, a saline extract of the organisms or the polysaccharid of the organisms. Control animals showed no tuberculin-like reaction forty-eight hours after the intracutaneous injection of the same products. The agent which causes reactions in sensitized animals appears to occur in the polysaccharide fraction of the extract. No constitutional reactions occurred.

BLUEFARB, Chicago.

FAT METABOLISM IN ACNE VULGARIS. EDWIN B. LE WINN and I. ZINGERMAN, J. Lab. & Clin. Med. **28**:191 (Nov.) 1942.

The Bloor method of determination of the cholesterol content of the blood was used as an indicator of the lipid content of the blood by the authors in an investigation of fat tolerance on 20 patients with acne vulgaris and 13 patients who served as controls. None of the patients used as controls showed any evidence of acne either present or past. The severity of the lesions in the patients with acne varied from a few well developed comedos and pustules on the forehead to extensive and active involvement of the forehead, face, shoulders, chest and back. Their ages varied from 11 to 29 years, and the duration of the disease was from one month to eleven years. The age limit of the patients used as controls was higher, ranging from 20 to 65 years. The authors felt they were justified in using these controls since advancing age causes only slight changes in the level of cholesterol in the blood. Most of the 12 female patients in the group with acne exhibited some menstrual disturbance.

Cholesterol has a dual relationship, as it is intimately associated with metabolism of fat and is chemically related to the steroid hormones, such as estrogen and androgen. It has been found that androgen will cause acne when given to women in large doses.

The procedure was as follows: A specimen of blood was taken after a twelve hour fast period. The patient then drank 500 cc. of 20 per cent cream, representing 100 Gm. of fat. Five specimens of blood were then obtained at intervals of one and one-half hours each and examined for total cholesterol. During the time of the test, each patient was allowed to take an occasional sip of water; most of the patients were ambulant, but activity was closely restricted.

In conclusion, the authors found that the fat tolerance of the two groups studied was within the accepted normal limits.

GELBER, Los Angeles.

ON THE NATURE OF ACUTE LUPUS ERYTHEMATOSUS. P. KLEMPERER, A. D. POLLACK and G. BAEHR, New York State J. Med. **42**:2225 (Dec. 1) 1942.

The authors, from a survey of the literature and from their own observations, conclude that the fundamental damage in lupus erythematosus is primarily in the collagenous tissue and that widespread visceral lesions are mere local manifestations of the basic damage to connective tissue, a severe manifestation of a colloidal imbalance.

THE MEDICAL ASPECTS OF ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS. E. C. REIFENSTEIN, New York State J. Med. **42**:2227 (Dec. 1) 1942.

Acute disseminated lupus erythematosus is a medical enigma. Since this diagnosis is sometimes made in the absence of cutaneous manifestations, it is difficult to accept this term as satisfactory.

The author sides with the pathologists who deny the existence of specific pathologic lesions. One is dealing with a systemic disease of unknown cause with a variable pathologic picture and a variable symptomatology. The terminology is confusing.

SULFONAMIDE THERAPY IN DERMATOLOGY: OBSERVATIONS IN TWO HUNDRED AND SIXTY-ONE CASES AT BELLEVUE HOSPITAL. M. J. COSTELLO, A. M. RUBINOWITZ and S. E. LANDY, New York State J. Med. **42**:2309 (Dec. 15) 1942.

Sulfonamide drugs were administered to 261 patients suffering from twenty-nine different dermatoses. Of those with erysipelas, lymphogranuloma venereum and chancroidal infections the majority were cured or improved.

The authors advise against the use of sulfonamide drugs orally in cases of localized superficial pyogenic infections, which will respond well to local application of 5 or 10 per cent sulfathiazole ointment.

Toxic reactions are relatively frequent, the most common being febrile reactions, dermatitis and bilateral conjunctivitis.

RONCHESE, Providence, R. I.

FALSE POSITIVE SEROLOGIC TESTS FOR SYPHILIS IN CHILDREN. MORRIS L. BRIDGEMAN and LEONARD D. JACOBSON, Northwest Med. **40**:325 (Sept.) 1941.

Bridgeman and Jacobson assert that there have been a greater number of false positive reactions to tests for syphilis in recent years, which may be due to the increased sensitivity and lessened specificity of the newer flocculation and precipitation tests.

In children, a false positive biologic reaction is most often associated with an acute infectious process with an elevation of temperature. Because of this it would be advisable to wait for a normal temperature before doing serologic tests.

It is entirely conceivable that, because of the nonspecific nature of the serologic tests, pathologic processes other than the spirochetal diseases can liberate a reagin-like substance which will give false positive reactions. Conditions reported as most commonly doing this are leprosy, malaria, infectious mononucleosis, trypanosomiasis, septicemia, scarlet fever, tuberculosis, jaundice, acute febrile conditions of varying nature, diabetes and varicella. Also it has been shown that false positive biologic reactions occur in a certain small percentage of perfectly normal persons showing no evidence of the presence of any infectious process.

Before a label of syphilis is placed on any child and, more important, before treatment is instituted, care should be taken to establish a definite diagnosis, by such criteria as: (*a*) positive physical findings in the child; (*b*) a definite history from either of the parents; (*c*) in the absence of these evidences persistently positive serologic reactions over a period of several weeks, rechecked by several different methods by different laboratories (the practice of beginning treatment on the sole basis of two, three or even four positive reactions is to be condemned; the value of serologic tests of the spinal fluid as confirmatory evidence is recognized, but false positive reactions can occur with the spinal fluid); (*d*) ruling out by the proper laboratory procedures of the presence of the more common diseases known frequently to cause false positive reactions, such as malaria and especially infectious mononucleosis, and (*e*) the use of Kahn's verification test as a possible aid in segregating the false from the true positive reactions.

The value of the various serologic tests used to diagnose syphilis is not questioned in this paper. The authors only wish to bring out that the diagnosis must be substantiated by further investigation, so that the label of syphilis is not placed on an innocent victim. Needless to say, the social and psychologic implications of syphilis of childhood should cause one to stop, look and listen whenever a positive reaction to a serologic test in childhood is obtained.

ROBERTSON, Omaha. [AM. J. DIS. CHILD.]

MOLES AND MALFORMATIONS OF THE SKIN. E. MEIROWSKY, Brit. J. Dermat. **54**:99 (April); 129 (May) 1942.

Man has become prone to have nevi and malformations of the skin by the factors of both domestication and phylogenesis. By the process of domestication new mutations have arisen in the germ plasm, producing general and circumscribed genodermatoses. Nevi are inherited and determined to the extent of nine tenths by the germ plasm. The unilateral formation of nevi is conditioned by the fact that genes can become effective only on one side of the body. The location in which nevi appear is determined by the regions which have played their part in the phylogenetic development (regions of clefts, of the spine, of the nipple, of sinus hairs and of markings of animal and human piebalds). All experimental and clinical investigations confirm the results of the analysis of normal skin; the germ plasm governs both its normal and its abnormal development. That is the elementary point from which research on moles must be continued.

A Case of Dermatomyositis. Muriel J. L. Frazer, Brit. J. Dermat. **54**:265 (Oct.) 1942.

A case of dermatomyositis is reported in which at autopsy the muscular lesions predominated, the cutaneous changes being relatively slight.

Bluefarb, Chicago.

Eczema and Dermatitis. V. Pardo Castelló and Berta Reand, An. brasil. de dermat. e sif. **17**:7, 1942.

The authors' review of the literature on the present conception of eczema and dermatitis shows the existing confusion in the terminology. A complete study of 209 cases showed that in 74 of them the condition was due to contact, in 20 with soaps, lotions or ointments and in 13 with nail polish. In other cases the condition was due to different causes, including tropical fruits, such as Mangos (manguifera indica) and mamoncillos (Melidia occidentale), and tropical plants, such as guao (Comocladia dentata). In 32 cases dermatitis was produced by internal disturbances; in 22 of these it was cured and in 1 improved. The conditions more commonly encountered were gastric, hepatic, intestinal, diabetic or nervous disturbances.

The authors conclude that it is necessary to return to the conception that eczema and dermatitis are a cutaneous reaction due to a number of local or general disturbances, allergy, chiefly by contact, being only one of them. Gastrointestinal and hepatic conditions, cholecystitis, enteritis and colitis are among the most frequent causes of eczema. The clinical entity of infantile eczema should disappear, as probably in only 2 per cent of cases of this entity are allergic phenomena of the hereditary and familiar type. The word "atopy," according to the authors, should be replaced by idiosyncrasy, or better, allergic idiosyncrasy.

Tuberculosis Cutis: Some Types Observed in Buenos Aires. Jose J. Puente, Rev. argent. de dermatosif. **26**:173, 1942.

The cases of tuberculosis of the skin observed in three different institutions in Buenos Aires from 1923 to 1942 are reviewed. The disease occurred in 0.28 per cent of all cases of cutaneous disease. Statistics twenty-five years ago showed the same incidence. For each case of lupus vulgaris, 5 cases of lupus erythematosus were observed. Roentgenologic examination of the lungs showed 6 per cent of activity in true tuberculosis of the skin and 11.7 per cent in tuberculids. In 30 per cent of the cases of true tuberculosis, lesions in evolution were noticed while such lesions were seen only in 1.6 per cent of the tuberculid group. Findings of preceding pulmonary lesions were more numerous (25.8 per cent) in the tuberculid group than in the true tuberculosis group (13.3 per cent).

The Field Laboratory Test of Briceño Rossi: A New Reaction for the Diagnosis of Syphilis. A. L. Briceño Rossi, Rev. san. y asist. social **7**:333 (June) 1942.

Briceño Rossi emphasizes the difficulty of the performance of the known serologic tests for syphilis in towns in Venezuela where laboratory facilities are meager. At the Institute of Hygiene, of which he is director, the author has used a new test which requires little equipment, not even a water bath. Its technic is somewhat similar to that of the Kline test. The blood is collected in a V-shaped capillary tube. It is centrifuged for two minutes with a hand centrifuge, and, by breaking the tube, the drop of serum is put on a glass slide. A drop of 10 per cent sodium chloride and a like amount of Kahn antigen are added. The ingredients are mixed with a toothpick and the reaction is immediately read. So far 1,277 tests have been made with serum from patients from different institutions, including patients with yaws and pinta. The results of 1,020 showed complete agreement with those of the Kahn standard test. It is interesting that the author's test gave fewer positive reactions than the Kahn standard test in cases of leprosy.

Cañizares, New York.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

UDO J. WILE, M.D., *President*

MICHAEL H. EBERT, M.D., *Secretary*

Oct. 21, 1942

Dermatitis Herpetiformis in a Child. Presented by DR. MICHAEL H. EBERT.

E. D., a white girl aged 3 years and 4 months, first noticed an itchy erosion in the pubic area six months ago. This was followed by a crop of tense bullae associated with intense itching. The bullae then appeared on the crotch, thighs, neck, arms and hands. She was first seen at Cook County Hospital four months ago. There were many tense bullae and erosions in these areas. She was treated with sulfapyridine, which rapidly controlled the eruption. At present a maintenance dose of 0.5 Gm. twice a day controls the eruption. A blood count showed 3,390,000 erythrocytes and 4,000 leukocytes.

DISCUSSION

DR. OLIVER S. ORMSBY: I suggest that the members discuss their experiences with sulfapyridine in treatment of dermatitis herpetiformis. I have used it for adults with good results. With its continued use the symptoms are held in abeyance.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: My colleagues and I have used sulfapyridine now in over 20 cases of dermatitis herpetiformis. Dr. Brunsting is preparing a report of this series, and without giving exact percentage figures I can say that in the Section on Dermatology at the Mayo Clinic we have had most striking results in a great many cases, decided improvement in the majority of cases and practically no failures. It is true that most of the patients must continue to take sulfapyridine to prevent a recurrence. Fortunately, some can be kept free of lesions with small doses given only every other day or even less frequently. For others, however, the dosage of sulfapyridine may have to be kept so high that one hesitates to continue use of the drug. We have tried all the other available sulfonamide compounds. Sometimes sulfathiazole works satisfactorily, and this is true also of sulfanilamide, but they do not work as well as sulfapyridine. We recently saw a patient who had an atypical dermatitis herpetiformis. He stated he could clear up the lesions in two or three days by taking sulfathiazole plus solution of potassium arsenite (Fowler's solution). Ten grains (0.65 Gm.) of potassium iodide given by mouth caused a flare in the dermatitis but without development of vesicles. He was then given sulfapyridine, and after he had taken 10 tablets the eruption had undergone complete involution. The response to sulfapyridine in borderline cases may almost be regarded as a diagnostic test.

DR. UDO J. WILE, Ann Arbor, Mich.: My only experience with sulfapyridine in the treatment of dermatitis herpetiformis is that the drug gave striking results for a time but when its use was stopped the eruption reappeared promptly. Perhaps I have not used it long enough.

DR. RUBEN NOMLAND, Iowa City: Knowing the advantage of sulfapyridine in dermatitis herpetiformis, my associates and I have tried pyridine hydrochloride, wondering if that component of the drug might be helpful. Unfortunately, pyridine has not given any response, and, as a matter of fact, we have had severe toxic reactions from it in the treatment of dermatitis herpetiformis.

The second thing I wish to say about this case is that here is a child with dermatitis herpetiformis of a special type, a type which I believe Dr. Tomlinson, of Omaha, reported (Tomlinson, C. C., and Cameron, O. J.: Juvenile Pemphigus: Effects of Germanin in Three Cases, ARCH. DERMAT. & SYPH. **38**:555 [Oct.] 1938) before the American Dermatological Association as a form of pemphigus, though I do not believe it is. I believe that dermatitis herpetiformis in children is entirely different from that in adults. I should like to hear Dr. Oliver discuss this case. I believe he has reported several cases of this type of dermatitis herpetiformis.

NOTE.—Further use of pyridine hydrochloride has shown less toxic reaction and promising clinical results.

DR. EDWARD A. OLIVER: About twenty years ago, I reported 3 cases of dermatitis herpetiformis in children from the Children's Memorial Hospital. I believe the prognosis for children is good for complete recovery, because one of the worst cases that I reported was that of a boy whom I have seen within the last two or three years, not with dermatitis herpetiformis but with another cutaneous disease. I had not seen him for a number of years and on questioning him about his dermatitis herpetiformis received the information that the eruption had cleared up entirely at about his tenth year and that he has never had any further trouble. As far as children are concerned, I believe the disease is self limiting.

As for sulfapyridine therapy, I have used it in about 6 cases, with excellent results. In 1 of the patients, with dermatitis herpetiformis confined entirely to the sides of the forehead and of two years' duration, the lesions cleared up in about two weeks' time. We are now watching him carefully and are giving him very small doses of the drug.

DR. MAURICE OPPENHEIM (by invitation): I have had good results in the treatment of dermatitis herpetiformis with acetarsone, particularly in children.

DR. M. H. EBERT: I did not have the heart to deny this girl the drug in order to make her a good specimen for this meeting. When first seen she had large eroded areas and bullae and there was some question whether the eruption might not be a severe pyoderma. After one or two observations my associates and I soon realized it was dermatitis herpetiformis.

The other reason for showing her was the fact that while we could control her lesions with sulfapyridine we wondered how long it would be wise to continue use of this drug. Evidently it does not cause distress, but it takes 1 Gm. a day to keep her in the condition she is in today. Perhaps it would be wise to change to acetarsone and then go back to sulfapyridine. I feel that in our experience at the Cook County Hospital the response to sulfapyridine is enough to enable us to make a differential diagnosis between dermatitis herpetiformis and other bullous lesions, including pemphigus. As time goes on we may find exceptions to that rule.

Dermatitis Repens. Presented by DR. F. E. SENEAR and (by invitation) DR. H. C. SCHORR.

C. B., a single woman aged 35, states that about one and one-half years ago, while washing dishes, she stuck her left finger with a fork. She now presents pyoderma of the distal portions of several fingers. The duration of this eruption is six months on the small finger, one year on the thumb and one and one-half years on the ring finger. One toe has been affected for the past one and one-half years.

DISCUSSION

DR. L. F. WEBER: I have had occasion to see a few persons suffering from dermatitis repens, and the oftener I see this disease the more doubtful I am of the diagnosis and certainly of the treatment.

DR. S. W. BECKER: I should call it acrodermatitis continua, which is one variety of dermatitis repens.

DR. UDO J. WILE, Ann Arbor, Mich.: My experience with this type of eruption and sulfonamide compounds has been happy. I not only give the drugs by mouth, but I use 5 per cent solutions of their soluble sodium salts in wet dressings. It has been my experience that dermatitis repens in the past has been extremely resistant.

DR. J. H. MITCHELL: This was not my impression of dermatitis repens, but in talking with Dr. Ormsby about it he told me he had a patient under observation and others of that character. Clinically today I see nothing about the case that I would diagnose as dermatitis repens.

DR. OLIVER S. ORMSBY: I stated to Dr. Mitchell that the patient had a peculiar paronychia with an associated resistant dermatitis on the fingers, which we had not classed as dermatitis repens. I have had much experience with dermatitis repens, and I did not consider this case as an example of that disease although there was a resemblance in the location and persistence of the lesions.

DR. FRANCIS E. SENEAR: I have no quarrel with any one who wishes to make a diagnosis of recalcitrant eruption if by that acrodermatitis continua is meant. We saw the patient for the first time yesterday. I called the disease dermatitis repens rather than acrodermatitis continua because of the uniformly pustular involvement of the nailbed. I feel that with extension of the process the picture would be that of a classic dermatitis repens.

A Case for Diagnosis (Erythema Induratum?). Presented by DR. M. H. EBERT and (by invitation) DR. M. OTSUKA.

R. C., a white girl aged 15, presents a deeply infiltrated plaque on the posterior surface of each leg at the junction of the middle and the lower third of the leg. These plaques appeared insidiously and were first noticed seven months ago. They cause no discomfort and have gradually increased in size. She has a history of rheumatic heart disease. She is well nourished and weighs 116 pounds (52.6 Kg.). On the right calf there is an irregular bluish red plaque, 3 cm. across, with slightly nodular surface. On palpation a much larger deep infiltrate involves the cutis and subcutis in an area 6 by 8 cm. The hardness is almost cartilaginous. A similar but smaller lesion is symmetrically located on the right leg.

Repeated determinations of basal metabolic rate have given results varying from —12 to —20 per cent. Intracutaneous injections of old tuberculin in dilutions of 1:100,000 to 1:1,000 gave negative reactions. The Kahn and Wassermann reactions of the blood were negative. Chemical examination of the blood, urinalysis and a roentgenogram of the heart and lungs all indicated normal conditions. The blood count showed 4,100,000 erythrocytes, a hemoglobin content of 77 per cent and 8,000 leukocytes, with a differential distribution of 68 per cent polymorphonuclear neutrophils, 26 per cent lymphocytes and 8 per cent monocytes.

Histologic examination of both lesions revealed that while the entire depth of the corium was involved, the major changes were in the deepest portion. Apparently the biopsy specimen did not reach the fascia. The elastica was largely destroyed in the upper part of the corium and entirely so in the deeper portion. There were numerous foci of cellular infiltrate, which were largest and most dense in the deeper part of the corium. The infiltrate was perivascular and in some areas was made up of plasma cells and in others of polymorphonuclear leukocytes, but in the deeper layers it was mixed, consisting of plasma cells, polymorphonuclears, histiocytes and connective tissue cells. The walls of some of the deeper vessels were edematous and infiltrated with polymorphonuclear leukocytes. Some of the deep veins were thrombosed and surrounded by a polymorphous infiltrate. In one section there was evidence of necrosis in the deepest portion. Stains for amyloid and mucin gave negative results.

NOTE.—After the meeting the patient was given a few doses of potassium iodide. Both lesions promptly broke down, leaving a deep necrotic ulcer which has shown little tendency to heal.

DISCUSSION

DR. CARL W. LAYMON, Minneapolis: In my opinion it was most difficult to make a diagnosis in this case. I did not think the lesions were erythema induratum. The possibility of lipogranulomatosis came to my mind, although I could not be certain that that was the correct diagnosis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. O'Leary and I and Drs. Barker and Allen, of the vascular service, have been much interested in a group of cases such as this, in which the disease simulates the clinical picture of erythema induratum but does not follow the same course or respond to various types of treatment used in erythema induratum. Histologic examination has shown no tubercle formation but has shown obliterative changes in the vessels and an acute perivascular inflammatory infiltrate of polymorphonuclear leukocytes. We have regarded some of these as cases of thrombophlebitis. In other instances the histologic picture is indistinguishable from that of periarteritis nodosa, although the clinical observations do not fit in with this diagnosis. We are uncertan as yet whether in these cases the changes are on an inflammatory or on an obliterative vascular basis. In studying this group of cases it is important to take a large and deep specimen for biopsy, going down into the subcutaneous tissue and taking a specimen about an inch and a half (3.8 cm.) long. Because of the large size of the specimen, it is important that the tissue be fixed for forty-eight hours instead of the usual twenty-four. I am not at all certain whether the case of the patient just presented by Dr. Ebert belongs in this group of cases.

DR. M. H. EBERT: This case has been a puzzle to us clinically and histologically. The histologic changes do not fit in with anything that I know of. Clinically, the lesions resemble erythema induratum, but there are many points of difference. The disease has persisted over a long period, seven months. The lesions have enlarged but have not broken down, and no new lesions have formed. All the various stains that we made for mucin and amyloid and other types of degeneration gave negative results. One would expect degeneration from the amount of infiltrate seen in this section. From the biopsy specimen which I studied, which is not as deep as the one here presented, I could see an obliterative endarteritis with an acute inflammatory reaction in the walls of the vessels and surrounding the walls of the vessels, a plasma cell reaction in the older areas. All of that gives no hint of the cause or pathogenesis of the disease. I think we shall have to await the results of research at the Mayo Clinic before we can give a name to this disease.

Bowen's Disease. Presented by DR. M. H. EBERT and (by invitation) DR. M. OTSUKA.

M. O. L., a woman aged 42, presents a cutaneous lesion on the right hip and a smaller lesion under the right breast of fourteen years' duration.

The lesion on the hip is a plaque 3 by 5 cm. with a polycyclic, slightly raised border. The surface is brownish red and slightly scaly. The other lesion, under the right breast, is smaller but similar.

The following changes were revealed by histologic examination: The epidermis was acanthotic, and the rete cells showed deviation in size as well as variation in the plaque and density of the nuclei. Clumping of the nuclei was present.

DISCUSSION

DR. M. R. CARO: I thought the section fitted in with the diagnosis of intraepidermal epithelioma.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: This patient took iron and arsenic as a child, and the question therefore arises whether these are not arsenical epitheliomas rather than true lesions of Bowen's disease, although the clinical appearance would be consistent with that which Bowen originally described. Bowen's disease is histologically a squamous cell epithelioma in situ, which is also true of the early stages of arsenical epithelioma. Although there is more vacuolation of the prickle cells in arsenical epithelioma, the changes are not great enough to distinguish between true Bowen's disease, senile keratosis or other precancerous dermatoses that I have enumerated many times in the past.

DR. RUBEN NOMLAND, Iowa City: I am not satisfied with the biopsy. I should like to see the serial sections to ascertain whether other forms of intradermal malignant growth do not appear in the section.

DR. M. H. EBERT: Some confusion arises in any discussion of Bowen's disease. The clinical syndrome of an extremely chronic, slowly progressing polycyclic scaling plaque originally described by Bowen was found to have a bizarre histologic picture. The rete cells, of varying sizes, present dyskeratosis, clumping of the nuclei and poikilokarynosis. This peculiar histologic picture is found in many different clinical conditions, including tar dermatoses and dermatoses following exposure to roentgen rays and changes following the intradermal injection of arsphenamine. Bowen's disease as a histologic entity is not uncommon and is now considered an intraepidermal carcinoma by some authorities. I believe this is clinically as well as histologically Bowen's disease.

Subungual Purpura Due to Neo-synephrin Nose Drops. Presented by DR. E. A. OLIVER and DR. S. J. ZAKON.

S. L., a white woman aged 37 years, was seen at Northwestern University on July 24, 1942 and received treatments for acute sinusitis. Since the treatments did not relieve her nasal congestion, on the advice of a friend she began to use 1 per cent solution of neo-synephrin hydrochloride. She used about 2½ ounces (75 cc.) of this solution from July 24 to September 30. About the middle of September she began to feel a numbness at the tips of her fingers, and later she noticed a discoloration of the tips of the fingers and the nails.

Examination on Sept. 30, 1942 revealed a purple discoloration of the tips of all the fingers and a deep blue discoloration of the nails. The fingers felt cold to touch.

She was told to stop the use of neo-synephrin, and the discoloration began to fade, so that on Oct. 14, 1942, when she was last seen, the color of the skin of the fingers and of the nails had returned to normal.

DISCUSSION

DR. M. H. EBERT: The first subungual hemorrhage due to a drug that I encountered was caused by acetylsalicylic acid. I was treating a man in the clinic for lupus erythematosus at the same time that he was being treated for tabes in the neurologic department. When the lightning pains came on his physician told him to take an unlimited amount of acetylsalicylic acid, 60 to 80 grains (3.9 to 5.2 Gm.) a day. He appeared one day with subungual hemorrhages which were rather startling. I learned that he was taking acetylsalicylic acid. When he discontinued the use of the drug the hemorrhages disappeared. I have never seen a hemorrhage due to neo-synephrin.

DR. L. F. WEBER: I should be willing, at least for the time being, to accept the cause, but I believe that a traumatic factor must be considered.

Women allow their nails to grow long. I have seen several persons with long finger nails which were repeatedly traumatized, and this resulted in subungual hemorrhage. This occurs in typists. It is likely that women who do their own housework cut the finger nails.

DR. RUBEN NOMLAND, Iowa City: I believe Dr. Oliver's diagnosis is correct, but I believe I have an explanation for it. This woman showed definite vasomotor spasm of the capillaries of the nail bed. When she held out her hand, the nails would turn white and then red, sometimes one nail and sometimes another. I believe she has vasomotor spasms with resulting hemorrhage. The vasomotor spasm is probably caused by the drug which she has been taking.

DR. S. J. ZAKON: Neo-synephrin hydrochloride, which has been in use since 1926, is a vasomotor constrictor which is active when administered by mouth. I imagine that the purpura is due to the fact that in putting the drops into the nose she swallowed a considerable amount. I was unable to find another instance of a sympathomimetic compound's causing purpura.

Mycosis Fungoides in the Tumor Stage. Presented by DR. M. H. EBERT and (by invitation) DR. M. OTSUKA.

L. M., a Negro woman aged 42, has had an eruption for eleven years, and since the onset she has been troubled with severe itching. At present there is practically universal involvement of the skin. There are hundreds of nodules varying from bean-sized growths to large tumors. On the back there are infiltrated plaques which still show a tendency to exaggeration about the follicles, giving a shagreen appearance to the skin. On the left leg there is a tumor the size of half an orange, with a depressed central ulcer. A large fungating ulcerated tumor is located on the right breast and a smaller one on the right jaw. Her palms are thickened and fissured. Examination of the blood showed 3,740,000 erythrocytes, a hemoglobin content of 63 per cent and 11,500 leukocytes, with a differential count of 59 per cent polymorphonuclears, 17 per cent eosinophils, 1 per cent basophils, 16 per cent lymphocytes and 7 per cent monocytes. The Kahn reaction of the blood was negative. A roentgenogram of the chest was essentially normal. Her basal metabolic rate was normal. Urinalysis, chemical analysis of the blood and an electrocardiogram indicated normal conditions.

Three years ago the peripheral blood picture was normal. A sternal puncture at that time revealed 25 per cent lymphocytic elements (normal number 3 to 5 per cent).

Lymphoblastoma? Presented by DR. OLIVER S. ORMSBY.

W. S., a man aged 68, has had a cutaneous disorder for five years. The eruption began on the feet and ankles and spread to other sites. Treatment of various kinds has had no effect on the disease. Itching has been intense and increased at night. At present there are numerous closely set, pinhead-sized, flat and conical papules irregularly disseminated over both upper and lower extremities, with a large patch situated in the left thoracic region. The skin is dry and in places presents moderate lichenification. There is also some hyperpigmentation. There is one enlarged gland in the left axilla. Examination of the blood was peculiar in that a differential count of white cells revealed 40 per cent polymorphonuclears, 30 per cent lymphocytes, 28 per cent eosinophils and 2 per cent monocytes. Lack of time has prevented further investigation.

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR. J. H. MITCHELL and (by invitation) DR. R. H. SCULL.

E. C. H., a Negro dentist aged 43, has had an eruption for two years, during which time he has visited a number of dermatologists and clinics. The trouble began in 1940, when he noticed an uncomfortable feeling around the shoulders and back while driving his car. Later his wife noticed a red spot on his left leg somewhat raised above the surface of the skin. Eventually there were others that became scaly and associated with itching, until the whole body with the exception of the face was involved. Recently the palms and soles have become scaly.

Examination reveals a large number of scaly and infiltrated plaques associated with raised erythematous infiltrated lesions. Also there are depigmented and horny macular lesions.

On examination the blood was normal except for a 5 per cent increase of eosinophils. The Wassermann and Kahn reactions of the blood were negative.

Three biopsies were made, one specimen being taken from a red infiltrated plaque, another from a scaly lesion and a third from a depigmented, horny area.

In the red infiltrated plaque, the epithelium was acanthotic. The polymorphous infiltrate, nodular in shape, consisted of multinucleated lymphoblasts, lymphocytes, a few mitotic figures, and plasma, giant plasma and endothelial cells. Here and there were some large cells with giant round, pale-staining nuclei. Special staining showed many elastic and collagenous fibers in the infiltrated area.

The other two sections were histologically the same, except for the type and amount of infiltrate. The depigmented area had the least amount of involvement, with horny plugs and little parakeratosis.

Mycosis Fungoides. Presented by DR. E. A. OLIVER and (by invitation) DR. S. M. BLUEFARB.

E. M., an obese white woman aged 44, first noticed an eruption about eight months ago, when a lesion appeared on the left flank. This has increased to its present size, which is about 7 inches (18 cm.) in length by 4 inches (10 cm.) in width, and there is a lesion about the size of a small egg on the right flank and a satellite lesion over the one on the left flank. The lesions are erythematous, nodular and ulcerative, and the border is serpiginous in some areas. There are no subjective symptoms such as itching or pain. There is a tendency for some of the lesions to heal spontaneously.

The blood pressure was 220 systolic and 138 diastolic, and the Kahn and Wassermann reactions of the blood were negative. A hemogram revealed 5,440,000 erythrocytes, 8,300 leukocytes and 14.7 per cent hemoglobin.

DISCUSSION

DR. A. W. STILLIANS: I observed only 1 case; it was the first case of mycosis fungoides in a Negro that I ever encountered. I should accept the diagnosis without any doubt.

DR. UDO J. WILE, Ann Arbor, Mich.: It appears to me that mycosis fungoides has changed its clinical characteristics, at least so far as my experience is concerned, in the last several years. This is a distinct impression and perhaps only a personal observation. In the many patients with this disease that I can recall having seen years ago, all of the lesions had reached the tumor stage and shortly thereafter the patients died.

I have seen but a single case of mycosis fungoides in the last ten years in which the lesions have gone beyond the stage of infiltration. The many lesions that have reached the infiltrated stage have all responded to a type of roentgen therapy which was not used two or three decades ago. At the present time I have under observation a number of patients with this disease who have been clinically well for several years, and all of them have had incredible amounts of superficial irradiation. It is my impression that the changing clinical picture in mycosis fungoides is due to the ability to use large amounts of superficial roentgen rays, which was not possible with the earlier gas tubes and more primitive forms of roentgen ray equipment.

DR. H. E. MICHELSON, Minneapolis: I think that in a case like this the first approach is clinical observation and then microscopic examination. I do not share Dr. Wile's view that mycosis fungoides or pemphigus is changing. I believe that one is apt to draw conclusions from the material at hand. There is no doubt that at times patients have lesions that one thinks are going to develop into mycosis fungoides and that recede under treatment; after long observation it is decided either that the disease was mild and aborted or that the diagnosis was mistaken. I have seen the same thing in pemphigus, and I remember Dr. O'Leary's stating last year that he thought pemphigus was becoming more mild. In my service, however, the last 4 patients died quickly. Prolonged observation is necessary before one may draw a final conclusion.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I agree with Dr. Michelson that dermatologists are still encountering severe as well as mild mycosis fungoides. There are many cases, as Dr. Wile mentioned, in which the disease stays under control with mild irradiation. My colleagues and I now feel that superficial unfiltered fractional doses are superior to filtered irradiation to the gland-bearing areas. Some patients have been kept free of lesions for ten to twenty years with irradiation. We have had other cases in which the lesions became resistant to roentgen rays, and in some cases which we have had Dr. O'Leary and I feel we have had good results with a combination of fever treatment and injections of ethyl chaulmoograte. One of these cases was presented at the San Francisco meeting of the American Dermatological Association. The cases presented today were cases of typical mycosis fungoides histologically as well as clinically, except that in 1 case there were a number of mitotic figures suggesting transition to lymphosarcoma.

DR. UDO J. WILE: I think you have the same view that I have, that mycosis fungoides is identified by a clinical rather than a specific microscopic diagnosis.

DR. FRANCIS W. LYNCH, St. Paul: In reference to Dr. Ormsby's case, the absence of generalized lymphadenopathy, the lichenoid papules and the high eosinophil count all point to the diagnosis of Hodgkin's disease, though it is obvious that the diagnosis has not yet been proved.

DR. S. J. ZAKON: The patient of Dr. Ormsby's has been under observation at Northwestern University for some time, and the clinical picture has not changed much. We made sections and blood counts. We removed a gland, but we never could establish a diagnosis of either lymphoblastoma or mycosis fungoides. It has always been a question whether it was a disseminated type of neurodermatitis or prefungoid mycosis fungoides.

DR. HAMILTON MONTGOMERY: By a typical histologic picture of mycosis fungoides, I refer to the early infiltrative stages, in which there is observed an infiltrate composed of multiple types of cells together with pyknosis and karyorrhexis of the individual cells and a tendency to form pseudo giant cells. From a purely pathologic point of view, in this stage the histologic changes are those of an inflammatory process and there are no appreciable number of mitotic figures. This is similar to the inflammatory picture presented in the early stages of Kaposi's sarcoma, which terminates as a true malignant neoplasm. In many cases mycosis fungoides may eventuate in any one of the lymphoblastomas, whereas in others mycosis fungoides remains true to type throughout the course of the disease.

DR. EDWARD A. OLIVER: Our patient appeared at our clinic about two weeks ago with a diagnosis of syphilis. After examining him carefully, we felt that the eruption showed many of the characteristics of mycosis fungoides of the d'emblée type. I am glad to hear Dr. Montgomery say that the sections substantiated that diagnosis. Up to a few years ago we felt that mycosis fungoides was rather uncommon in Negroes, but in the last few years we have a number of them with the disease. I thought the case of the Negro dentist was the most interesting of the 4 cases.

DR. M. H. EBERT: This woman has been shown before to this society. At that time she presented lesions of the infiltrative stage. She was shown today for two reasons: first, because mycosis fungoides is not common in Negroes (this is the second case I have seen; the first had a fatal outcome); second, because I think it is classic mycosis fungoides terminating in the tumor stage without any changes in the peripheral blood.

DR. OLIVER S. ORMSBY: I should like to say a word about mycosis fungoides. My experience is similar to that of Dr. Wile. Years ago I had a number of patients with mycosis fungoides with fungating tumors, some of them pronounced. I have not seen one of this type for several years. My colleagues and I have treated several patients with the plaque type of lesions with roentgen rays and have been able to control the disease over a period of several years.

Concerning my case, I am glad to hear Dr. Zakon's report. I do not believe a microscopic section in this case would help the diagnosis. Because of the history and the type of lesions, I shall consider the lesion a lymphoblastoma, with a probability of its being Hodgkin's disease.

DR. J. H. MITCHELL: I thought our case was interesting in many ways. As Dr. Oliver has pointed out, it is interesting to see in 2 Negroes a disease formerly thought to be rare in that race. We saw this patient for the first time last Friday. He was brought in by Dr. Scull. He is a dentist. He was treated here in Chicago and then later went to the Mayo Clinic and was seen there. His case does not present a typical clinical picture of mycoses fungoides but three types of lesions—pigmented, depigmented and exfoliative—all interesting. We have sections of each.

Livedo Reticularis (Syphilis). Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS and DR. JAMES GOODFRIEND.

M. C., a Negro baby aged 5 months, presents a generalized residual pigmentation involving the body and extremities, a condition which has been present since the child was 3 weeks of age.

This baby was first seen when about 3 weeks old and before treatment was instituted, and at that time the pigmentation was reticulated and of a deep sepia color and involved the entire integument.

There is a history of syphilis in the mother, who was under treatment in the early period of her pregnancy, and she is reluctant to speak about her treatment or is evasive. However, the Wassermann reaction of the blood of the mother and of the child was positive (4 plus).

The baby was given the five day intensive treatment at the Children's Hospital, and the pigmentation has gradually faded to the point where it is hardly visible now.

DISCUSSION

DR. M. H. EBERT: I do not believe that this is livedo reticularis on a syphilitic basis. I think that the infiltrate would be greater and would not be absorbed as quickly as it was in this child. I think it is postarsphenamine pigmentation. The location of the pigmentation is determined by the slowing of the circulation between the areas supplied by the terminal arterioles. It is this slowing of circulation in the areas between arborescent terminal arterioles which gives the reticular pattern in cutis marmorata, in which there is a spasm of the arterioles on exposure to cold.

I do not think there is any evidence in this case of syphilitic infiltration of the arterioles.

DR. MAURICE OPPENHEIM (by invitation): I have seen some cases of livedo reticularis presented by Ehrmann, who first described it. He stated the belief that syphilis was the cause

and found plasma cell infiltration around the arterioles. This was the cause of this type of mottled skin on certain areas. The little Negro child presented by Dr. Omens has a totally different rash. Livedo reticularis is symmetric and occurs mostly on the extensor surfaces of the extremities. The color is like that of mottled skin but is permanent; by raising the arms, for instance, the color is paler and in some places disappears totally. Livedo reticularis is not influenced by any specific treatment; it is permanent. Syphilis is not the only disease which causes livedo reticularis; one finds the same eruption in tuberculosis and in lupus erythematosus, sometimes after acute infectious diseases and in children after measles and scarlet fever. I agree with Dr. Ebert that this patient does not show this picture. Livedo reticularis cannot be recognized in Negro patients. It is a disease caused by involvement of the arterioles and smaller arteries in the skin; it never spreads over the whole body; it is mostly on the extremities, and it is symmetric. There may be some inherited basis for the development of this rare disease.

Dyskeratosis Bullosa (So-Called Benign Familial Pemphigus). Presented by Dr. S. W. Becker.

Mrs. C. S., aged 42, first noticed a blister on the back of the neck at the age of 21. It ruptured spontaneously, and an erythematous plaque persisted. The eruption later appeared in both axillas. It has persisted intermittently since that time with no particular seasonal variation, although it is aggravated by heat. No other member of her family, immediate or remote, has a similar eruption. She has three brothers and three sisters, all of whom are living and well. Physical examination revealed no abnormality except a fairly low blood pressure, 114 systolic and 82 diastolic.

She was observed at the University of Chicago Clinics for two and one-half years (1936 to 1939). The newly appearing lesions were diagnosed as impetigo. Older ones were considered to be lichen simplex chronicus.

The patient was again seen on Aug. 15, 1942, at which time she presented plaques on both sides of the neck, in the axillas and in the groins. The plaques, which were several centimeters in diameter, showed vesicles or bullae at the borders, with crusting and scaling toward the centers. A diagnosis of dyskeratosis bullosa was made. At the present time she presents two lesions of this kind on the left side of the neck.

Microscopic section showed various stages in the formation of a bulla in the midportion of the epidermis, varying from slight acantholysis to a moderately large fully developed collection of fluid containing fibrin and polymorphonuclear leukocytes. The papillae and superficial dermis showed moderate intravascular and perivascular collections of leukocytes (polymorphonuclear). No definite dyskeratotic cells were seen in the epidermis.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: This looked to me, as far as I could see, like mild dermatitis herpetiformis. I wonder why the disease was classified as benign familial pemphigus, because there was no history of other members of the family having had it.

Dr. Francis W. Lynch, St. Paul: I agree with Dr. Becker's diagnosis, though I am not sure how the disease should be classified. I do not think it is a mild form of pemphigus or dermatitis herpetiformis. The dyskeratosis favors a relationship with keratosis follicularis, as does the response to treatment with vitamin A in some reported cases and in 1 case in my practice. In another case I observed a temporarily favorable response to sulfathiazole, but later there was a relapse in spite of treatment. The areas of predilection, the histologic structure and the absence of itching argue against classifying the disease with dermatitis herpetiformis. I think it had better be regarded as a distinct entity until more cases have been studied and more knowledge gained.

Dr. Hamilton Montgomery, Rochester, Minn.: I think this is a case of benign familial pemphigus. In the paper written by Frank and Rein (Arch. Dermat. & Syph. **45**:129-151 [Jan.] 1942) all the discussers except Goodman and Ellis were opposed to grouping this condition with Darier's disease. Rein reported a case from New York in which there was no history of familial occurrence, and I presented such a case a week ago at a meeting of the Minnesota Dermatological Society in Rochester. This, I believe, is the third case with no history of familial occurrence.

Dr. Udo J. Wile: The patient stated to me that these lesions definitely itched.

Dr. S. W. Becker: I think the similarity of this disease to dermatitis herpetiformis is reflected in the name which Ayers and Anderson gave to it, "herpetiform dermatitis repens." They recognized the spreading nature of the lesions. I think it illustrates a situation which is seen frequently. All of us must have seen patients with a similar disease in the past. As a matter of fact, this patient has been seen by several Chicago dermatologists. It is not

until somebody calls attention to the peculiarity of the disease that one notices it in practice. This is the second patient I have seen who reported that there was no history of familial occurrence. The microscopic pictures have been the same for all, whether there was a familial history or not. I think every one agrees that the disease has no connection with pemphigus. It may possibly be a variety of dermatitis herpetiformis. There were no dyskeratotic cells in this particular lesion. It was an early lesion, but it did show acantholysis and other changes which are characteristic for this particular disease.

DR. M. H. EBERT: I wonder whether it would be well to try treatment with sulfapyridine for this variety of dermatitis herpetiformis.

Tuberculosis of the Skin. Presented by DR. I. M. FELSHER (by invitation) and DR. MARCUS R. CARO.

F. M., a white girl aged 8 years, was first seen in the dermatologic department of the Mandel Clinic (Michael Reese Hospital) on Aug. 15, 1942. At that time she presented on the upper and lateral aspect of the left leg a well defined circular reddish brown infiltrated lesion about 0.7 cm. in diameter, of two or three months' duration. The center of the lesion was depressed and scaling, and the border was elevated and composed of small papules, about 1 or 2 mm. in diameter. No apple jelly macules were visible under the diascope. In the left groin there was a tender firm mass about 5 by 3 cm. consisting of coalescing enlarged lymph glands.

About two months before that time the patient was seen in the pediatrics department, where the lesion was described as a "small indolent vesiculopustule of one or two weeks' duration." While under our observation the lesion has progressed slowly in size (1 by 1 cm.), and recently brown macules have become evident under the diascope. The mass in the groin has broken down, with subsequent ulceration and drainage.

The mother of the patient was under observation in the same clinic from 1930 to 1942 because of an inactive focus of pulmonary tuberculosis. She died in July 1942, of metastatic carcinoma of the breast. The little girl had been in intimate contact with her mother, having frequently slept with her in the same bed.

The results of urinalysis were normal; the serologic reaction for syphilis was negative, and the blood count was within normal limits. Smears from the mass of enlarged glands in the left groin revealed tubercle bacilli. The Mantoux reaction was positive on Sept. 14, 1942. A report of the roentgenogram of the chest on October 12 stated: "Both hilar shadows are accentuated, and there is a suggestion of nodularity. Hazy markings extend into the proximal pulmonary field bilaterally, being most distinct below the medial ends of the clavicles. It is impossible to rule out an active childhood pulmonary tuberculosis."

Histologic examination of tissue removed from the lesion on the leg on October 12 revealed acanthosis and edema in parts of the epidermis. In the upper portion of the corium there was an infiltration of inflammatory character consisting predominantly of lymphocytes, a few epithelioid cells, histiocytes, fibroblasts and a few plasma cells. Deep in the corium and extending into the subcutaneous tissue was a nodule containing many epithelioid cells arranged in nests forming tubercles. There were also lymphocytes and fibroblasts. The connective tissue in general was edematous in places.

A Case for Diagnosis (Dermatitis Factitia? Neurotic Excoriations? Tuberculids?). Presented by DR. S. W. BECKER.

Mrs. F. M., a housewife aged 38, has had an eruption on the face, left leg, right arm and back of the neck for four years. According to her history, the initial lesion is a pruritic papule which becomes excoriated from slight trauma, such as is experienced during bathing. Overexposure to sunlight is followed by lesions for weeks. After healing, a prominent scar results. New lesions appear constantly. She has consulted several dermatologists, who told her that the lesions were caused by "nerves" or constituted a "neurosis."

In the aforementioned areas were lesions varying from erythematous papules with pale necrotic centers or hemorrhagic crusts to atrophic, noncontractile scars. A tuberculin test with purified protein derivative in an amount corresponding to a 1:50,000 dilution of old tuberculin gave a negative reaction. A lesion alleged to be only two days old was removed from the right arm. It was a papule 0.75 cm. in diameter with a brilliant erythematous periphery and a pale, necrotic center.

Histologic examination showed the center of the lesion to be covered by a fibrinous, homogeneous mass in which could be seen necrotic epithelial cells. Beneath the crust was an infiltrate of polymorphonuclear leukocytes, round cells and fibroblasts. The normal epidermis at the edge of the crust was hyperkeratotic and parakeratotic.

Lupus Vulgaris with Pulmonary Tuberculosis. Presented by DR. E. A. OLIVER and (by invitation) DR. S. M. BLUEFARB.

N. S., a white woman, was previously presented twice before the Chicago Dermatological Society (ARCH. DERMAT. & SYPH. **46**:600 [Oct.] 1942; ibid. **47**:449 [March] 1943) with a diagnosis of lupus vulgaris with pulmonary tuberculosis. About five months ago treatment by inhalation of a tuberculous broth culture was started. Each cubic centimeter of this culture contains 5 mg. of dead tubercle bacilli in solution of sodium chloride. While she has been receiving this form of therapy, there has been an improvement in her eruption.

DISCUSSION OF PRECEDING THREE CASES

DR. H. E. MICHELSON: In the first case the mother had tuberculosis, the roentgen changes in the chest are suggestive and there is a draining sinus. I think all will agree that this is an external inoculation type of tuberculosis, and it does not make such a great difference whether one calls it primary or not; but it is a compliment to the group here that such a diagnosis was suspected and verified, for I am sure that in many places tuberculosis would not even have been thought of.

The case of Dr. Oliver's is most striking. There can be no question about the diagnosis of lupus vulgaris, but to see such great improvement with a form of treatment which one might term biologic is gratifying. If in all cases lupus vulgaris should respond to this treatment, then maybe in fifteen years' time it will be said that lupus vulgaris has changed, for when there is an effective treatment for any disease the terrors of that disease diminish.

I should like to discuss Dr. Becker's case, because I think the diagnosis is neurotic excoriations. The patient states that she has been married, is divorced and has two children. She was born in Canada, and with her former husband traveled around a great deal so that she established no permanent ties. A similar history is elicited from persons who display neurotic excoriations. They have not the security of a fixed environment or group of friends. She states that she has been a sleepwalker since childhood and that this continued until she became sleepless and that now she has been receiving sedatives and feels great need for this drug. I am much against the indiscriminate use of sedatives, and, although there are times when they must be used, certainly a person with neurotic excoriations is the last one to whom I should administer a barbiturate, because the chronicity of the disease would lead to tremendous dosage. The proper treatment of neurotic excoriations is hard to decide on. I believe in many instances the aid of a sympathetic psychiatrist is necessary, and when I say sympathetic I mean a psychiatrist who is sympathetic with dermatology.

DR. EDWARD A. OLIVER: After our last meeting I sent Dr. Michelson a colored picture and the microscopic slide. What did you think of that?

DR. MICHELSON: I agreed with your diagnosis.

DR. OLIVER S. ORMSBY: During the last several months I have had several conversations with Dr. Irons about this treatment. He has had promising results, and the case presented by Drs. Oliver and Bluefarb shows the treatment to be effective against a most resistant disease.

DR. THEODORE CORNBLEET: In the Tice Laboratory, whose function it is to produce BCG vaccine (bacillus of Calmette and Guérin, a tubercle bacillus of low virulence), it was noted that some persons who reacted to 0.001 mg. or less of old tuberculin had symptoms of chills, fever and cough after exposure to fumes of boiling vaccine. Such responses abated, as did the degree of reactivity to tuberculin, after repeated exposures. Experimentally, partial reduction of reactivity to tuberculin was observed in guinea pigs which were subjected to daily exposures to such fumes. Some 30 patients with active pulmonary tuberculosis who were exposed to graded doses of fumes from boiling vaccine did not exhibit untoward symptoms as a result of the procedure. Several patients with tuberculous iritis have shown some clinical improvement following this type of treatment. My acquaintance with these facts came from Dr. Rosenthal, whom I asked to cooperate in undertaking some experimental therapeutic studies on cutaneous tuberculosis. It occurred to me that BCG vaccine might be of some service in the treatment of this disease. Since then Dr. Rosenthal and I have been using inhalations of BCG vaccine in treating a number of patients with tuberculosis of the skin and tuberculids. The results have been gratifying but not spectacular. They take months to achieve but compare favorably with those obtained with other methods with which I am acquainted. Naturally, in the United States only a few physicians have had extensive experience with cutaneous tuberculosis, and I am not one of them. Nonetheless, I believe that inhalations of BCG vaccine have definite promise as a therapeutic method for these cutaneous infections. Incidentally, this method has not been of any benefit in treatment of sarcoidosis.

DR. UDO J. WILE, Ann Arbor, Mich.: Is the broth heated to a high degree?

DR. THEODORE CORNBLEET: The BCG emulsion is heated to boiling and kept simmering at nearly that temperature. Glass beads are placed in the flasks containing the vaccine emulsion to decrease the chance of sudden puffs of the boiling material spurting into the patient's face. Some patients have used commercial inhalers that can be bought at most drug stores. In the beginning, therapeutic periods last a few minutes. They are progressively lengthened. Veteran patients inhale for half an hour twice a day.

DR. MINNIE O. PERLSTEIN: I should like to add 1 case which Dr. Cornbleet did not mention, that of 1 of his patients with papular necrotic tuberculids. This patient has been married five years and was sterile. She had a tremendous mass in the pelvic cavity, believed to be tuberculous salpingitis.

On surgical exploration, the mass was found to be retroperitoneal and consisted of all the pelvic organs as well as a coexistent mesenteric adenitis. Postoperatively, there was an exacerbation of the tuberculids. At this time she was given broth therapy, being one of the first patients so treated. Her general condition improved; at the present time she is pregnant, and the obstetrician is unable to feel the mass.

DR. MAURICE OPPENHEIM (by invitation): The first is a case of typical scrofuloderma; the irregular margins, the undermined margins, the bluish surroundings without inflammatory reaction and the scant secretion prove this diagnosis.

When I first saw Dr. Oliver's patient I did not believe the disease was lupus vulgaris; it looked unusual to me. Dr. Oliver kindly sent me the slides of the case, which showed without doubt the typical histologic picture of lupus vulgaris.

Dr. Becker's patient seems to have tuberculosis papulonecrotica or a self inflicted lesion. A self inflicted scar is irregular, sometimes in stripe form sometimes starlike. Today I saw a patient with self inflicted lesions. The scars were star-shaped and were almost of the same size and same form. The scars of a papulonecrotic tuberculid are round, regular in shape and different in size. The base is flat, and the surroundings are sometimes pigmented. They are located on the extensor surfaces of the extremities and on the face.

DR. RUBEN NOMLAND, Iowa City: I wish to agree with Dr. Michelson that Dr. Becker's case is a typical case of neurotic excoriations, which is encountered only in women in three phases of life: most frequently at the menopause, less frequently at puberty and fairly frequently in pregnancy. I believe they have a primary itching lesion which they scratch. I hesitate to put the disease on a purely neurotic basis. I am hoping that those persons who are studying the glands of internal secretion will give some help.

DR. M. H. EBERT: I believe that Dr. Becker's patient has neurotic excoriations. She has a complete hysterical anesthesia of the pharynx. I think this always accompanies neurotic excoriations as well as factitious dermatitis.

DR. I. M. FELSHER (by invitation): Dr. Caro and I considered that our patient had the inoculation type of tuberculosis, and as we watched the course of the disease we thought that it fitted well into that picture. Unfortunately, no tuberculin test and no roentgenograms of the chest were made before the appearance of the cutaneous lesions. Since a recent Mantoux reaction was positive and the report of the roentgenogram of the chest did not rule out completely the possibility of childhood pulmonary tuberculosis, it is difficult to say whether the lesions on the skin or the pulmonary involvement came first. The clinical course of the cutaneous lesions, however, supports strongly the possibility of the inoculation type of tuberculosis.

DR. S. W. BECKER: When I first saw this patient I was certain that she had neurotic excoriations, but as I saw her repeatedly I thought it was a factitious dermatitis and that she was producing the lesions without being willing to admit it. The microscopic section reveals a localized necrosis of the epidermis which is so superficial that I doubt whether it could be a tuberculid. The recent lesion which was removed and which we studied was alleged to be only of two days' duration but showed changes under the microscope which indicated that it had been present for a much longer period. I believe they are either neurotic excoriations or a feigned eruption. The patient is not willing to admit that the lesions itch or that she manipulates them. While I believe she is producing them, I wonder whether they should be called neurotic excoriations.

DR. EDWARD A. OLIVER: I want, first of all, to answer several of the statements that have been made and then to explain in a few words what this treatment is. The patient is not regarded as cured, but I am sure those who saw this girl five months ago will agree that she has improved a great deal.

This method of treatment was originated by Dr. Rosenthal and Dr. Irons and used successfully by Dr. Irons in the treatment of 2 patients with tuberculous iritis, a condition that has resisted many kinds of treatment.

Dr. Rosenthal has charge of a laboratory where he is engaged in the vaccination of children against tuberculosis. He uses BCG vaccine, and he is using it with a great deal of success. Some time ago it was noticed that often the laboratory workers became ill, generally over Sunday and Monday. They would have fever and a cough, would vomit and would be ill for several days. Later it was found that after such an attack their reaction to tuberculin was greatly reduced. It was later learned that workers in other laboratories were having similar experiences, and it was discovered that these attacks occurred shortly after they had been engaged in boiling up the used glassware with its cultures on Saturday afternoons.

Believing that these attacks were due to inhalation of fumes given off by the boiling of old cultures, Dr. Rosenthal and Dr. Irons experimented with guinea pigs, enclosing them in boxes and arranging the apparatus so that for a certain period each day the guinea pigs would breathe these fumes. After several weeks the guinea pigs were unharmed, but they, too, showed a decided reduction in their sensitivity to tuberculin. Cautiously, then, the treatment was given in 2 cases of tuberculous iritis. In both of them the disease was of long standing, and both patients reacted favorably. Knowing this and realizing that all other methods of treatment which had been tried for this girl had failed, I decided to try the inhalation treatment. She has been taking the treatment for five months and is now inhaling for forty minutes a day. She complains that this is making her ill; so I am suggesting to her that she reduce the time to twenty-five or thirty minutes daily.

The material used is a suspension of 5 mg. of dead tubercle bacilli in 1 cc. of solution of sodium chloride. The patient for the first few days inhales the suspension cold, at first taking only a whiff of the mixture and then gradually increasing the time of the inhalation. After a week or ten days, the suspension is heated on an electric plate, and the time is gradually increased from day to day.

The originators of this method of treatment realize that it is yet too early to make any claims for it. They offer it for what it is worth. I am glad to know that Dr. Cornbleet is using it in some selected cases.

Elephantiasis of the Vulva of Undetermined Cause; Furrowed Tongue; Perlèche.
Presented by Dr. Ruben Nomland.

A girl aged 16 has an enlargement of the vulva which was first called to the attention of her mother about fourteen months ago. Thereafter the enlargement was progressive and continuous until it reached the present size. It has remained the same size or possibly has regressed slightly during the past six months. In addition to this, the child has had a furrowed tongue all of her life and has had perlèche for years.

Examination of the genitalia reveals that both labia majora and the clitoris are red and edematous, with a moderate amount of white maceration in the folds. The right labium is about 8 by 2 cm., and the left is approximately half that size. The clitoris is so thickened as to be almost unrecognizable. The labia minora show some thickening. General physical examination showed a slight degree of malnutrition, but aside from that nothing abnormal was found.

The Wassermann reaction was negative, and Frei tests performed with human and egg yolk antigens gave negative results. Cultures of material from the cervix did not yield Neisseria gonorrhoeae, but beta hemolytic streptococci were obtained.

The child took sulfanilamide for a period of eight weeks or more, with only slight improvement. An eruption from the sulfanilamide developed on exposure to sunlight, but this was transitory.

DISCUSSION

Dr. Theodore Cornbleet: I thought perhaps this might be an instance of vitamin B_2 deficiency. In my experience few patients with perlèche get well from administration of riboflavin. An exception to this was a sailor whom I observed who had the classic syndrome such as is described by the vitamin experts. He responded promptly to the administration of riboflavin. He had an eruption similar to that present in this patient—perlèche, cheilitis and inflammation about the eyelids. I do not know what connection the vulvar elephantiasis in the present patient has with the changes on the face and lips.

Dr. Udo J. Wile, Ann Arbor, Mich.: Would you say that the disappearance of a lesion of the kind you described after vitamin therapy is definite proof of the fact that the patient had avitaminosis?

Dr. Theodore Cornbleet: Certainly not. There is a growing literature showing a broad, interdependent relationship among vitamin requirements and consumption, the endocrine glands and various diseases and pathologic states and intoxication. The situation may be compared

to that of a tripod, which falls with the removal of any leg. One does not necessarily remove the underlying endocrine disturbance by proper attention to nutrition even though the presenting syndrome is ameliorated.

DR. M. H. EBERT: This appears to be a lymph stasis in the vulva. There are some enlarged glands, considerably enlarged on the right side and not so much on the left. That would likely be on the basis of infection. One of the possibilities would be tuberculosis. The history did not state whether this girl had been studied from the point of view of tuberculosis. The only other possibility would be a streptococcic infection, even though she has no history of this organism's being found.

DR. RUBEN NOMLAND: I feel that the perlèche and the lesion on the tongue are entirely independent of the lesion in the vulva. The patient was completely studied in the department of pediatrics by Dr. Jeans, who is an authority on vitamins, and he felt that her diet was sufficient. In the general examination, it was his opinion that she was not unnourished but was retarded mentally. Because the mother read the history I did not state that the girl has masturbated since puberty. I believe she has a furrowed tongue. She has perlèche, for the corners of the mouth are continually wet with saliva. Dr. Mitchell has shown that persons in whom the angles of the mouth are wet with saliva always have perlèche.

The lesion of the vulva is inflammatory, essentially an elephantiasis nostras. There is no lymphedema, as Dr. Ebert indicated. I feel that elephantiasis nostras is the diagnosis. I hoped that some one would suggest that a plastic operation be performed. I think the process is inactive.

Lupus Erythematosus. Presented by F. E. SENEAR, DR. M. R. CARO and (by invitation) DR. P. K. WEICHSELBAUM.

R. G., a white woman aged 37, first noticed a small papule behind the right ear in April 1942. The eruption spread gradually to involve the present sites. Exposure to sunlight did not affect the lesions in any way. There was intense itching.

Examination of the urine showed a trace of albumin. The reaction to a tuberculin test with a dilution of 1 to 10,000 was positive. Examination of the blood showed the hemoglobin content to be 65 per cent, erythrocytes 3,700,000 and leukocytes 7,500, with a differential count of 31 per cent lymphocytes, 68 per cent neutrophils and 1 per cent monocytes.

The eruption involves the "V" area of the neck, the retroauricular areas with extension to the scalp, the back of the neck, the inner surface of the conchae of the ears and the extensor surfaces of the forearms. The lesions are dry, scaly, sharply circumscribed, erythematous patches and confluent papules varying from pinkish to violaceous red. There is no follicular accentuation or plugging and no evidence of atrophy.

Histologic examination of a section taken from behind the ear showed a thin non-nucleated scale. There was a slight edema in the basal layer. The vessels in the corium were dilated. In the upper part of the corium and about the blood vessels and follicles there was a dense infiltrate composed chiefly of lymphocytes. The Weigert stain showed elastic fibers to be entirely absent from the upper part of the corium.

DISCUSSION

DR. M. H. EBERT: On first glance the annular lesion looked something like granuloma annulare. Clinically it is unusual, but it seems to be lupus erythematosus.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The sections show a great deal of shrinkage of tissue, which makes histologic interpretation difficult. Whereas the histologic changes suggest lupus erythematosus, the clinical appearance does not. In regard to lupus erythematosus profundus the question arises whether in Negroes one has lupus erythematosus and sarcoid in the same patient or a form of hematogenous tuberculosis. Dr. Nomland has emphasized that tuberculosis in Negroes is different from what it is in white persons. In the case presented today it is possible that one may be dealing with both lupus erythematosus and sarcoid—tuberculosis, if one regards a sarcoid as being of tuberculous causation.

DR. UDO J. WILE, Ann Arbor, Mich.: I think this is lupus erythematosus, but I do not know why, except that it looks more like that than anything else.

DR. M. R. CARO: I think that histologically as well as clinically the case deviates from the usual picture of lupus erythematosus. The histologic picture, however, also tends to rule out other diseases which might be suggested by the clinical appearance. There is nothing in the section to suggest sarcoid or granuloma annulare. There are follicular plugging, intracellular edema in the basal layer and perivascular infiltrate, all of which could fit in with an atypical lupus erythematosus.

Sarcoid (Miliary). Presented by DR. S. W. BECKER.

Mrs. H. M., a housewife aged 53, first acquired a brownish red maculopapular eruption on the forearms four years ago, during her menopause. Occasional pruritus was present. The lesions were more noticeable in winter than in summer. There was no history of ingestion of drugs except occasional ingestion of a proprietary preparation of phenolphthalein for constipation. Her general health had been good except for arthritis of the fingers for two and one-half years. There was no known exposure to tuberculosis. The patient drank raw milk during childhood.

When the patient was first seen, in May 1940, the extensor surfaces of both forearms were covered by a maculopapular eruption consisting of lesions 3 mm. in diameter, faintly erythematous and yellowish and showing apple jelly color on diascopic pressure. General examination revealed no other abnormalities. A roentgenogram of the chest showed pronounced calcification about the right hilus. A blood count showed 6,700 leukocytes, with a normal differential count, and 4,310,000 erythrocytes. The hemoglobin content was 76 per cent. A microscopic section showed small perivascular collections of round cells and histiocytes in the subpapillary layer of the dermis.

The eruption disappeared completely under therapy with a gold compound. Three months later lesions appeared at the borders of the previous plaques; therapy with a gold compound again was followed by disappearance. The eruption recurred in January 1942. When she was seen in August, lesions were present on the forearms, hands, face and neck; they were 0.5 to 1 cm. in diameter, with sufficient elevation of the border that many of them appeared annular. Microscopic section showed the epidermis to be thinned, with disappearance of the interpapillary processes. In the superficial dermis was a loose perivascular lymphocytic infiltrate. Giant cells were present in the periphery of the infiltrate and in between the collagen fibers away from the blood vessels.

Sarcoidosis. Presented by DR. OLIVER S. ORMSBY.

Miss L. M., aged 35, has been presented before this society on two occasions, first, in January 1937 (ARCH. DERMAT. & SYPH. **36**:635 [Sept.] 1937) and again in October 1939 (ibid. **41**:591 [March] 1940). When she was originally presented, brown plaques and nodules were situated on the face, forehead and arm. There was some adenopathy and a spina-ventosa-like enlargement of one finger. The tonsils were apparently normal. In 1939, when she was shown the second time, there had been much improvement. Since that time an exacerbation has occurred, in which a number of new lesions developed, old lesions became enlarged and new involvement of the bone developed.

During the years arsenic has been used by injection and by mouth, tuberculin by injection and gold sodium thiosulfate by injection, and numerous vitamins have been given. Beginning in December 1941, injections of chaulmoogra oil were instituted. This oil was given in the form of ethyl chaulmoograte. The injections were given once a week intramuscularly and in gradually increasing doses until 12 cc. of the material was used. This made a great improvement in the lesions. At present there is moderate activity over much of the face and forehead, with some lesions on the upper extremities and some evidence of involvement of bone in the fingers.

The patient is presented to show the improvement obtained by the chaulmoogra oil derivative.

DISCUSSION ON SARCOIDOSIS

DR. H. E. MICHELSON, Minneapolis: I believe both patients have sarcoidosis, and it is interesting to note that 1 patient was treated with gold and the other with chaulmoogra oil and in both instances improvement has been decided. One must realize that sarcoid lesions may disappear without treatment and that at times this can happen in a short time. It is queer that one accepts gold as a treatment for so many conditions that are suspected to be of tuberculous origin and then deduces that because of the improvement the cause must be tuberculosis. On the other hand, if one uses chaulmoogra oil one might deduce that the lesions were akin to leprosy. Certainly, the more recent works have thrown no light on the causation of sarcoidosis. It seems to be more and more a syndrome and certainly not a disease which is characterized by the involvement of a single system.

DR. S. W. BECKER: My patient was shown before this society previously, although the report was not written up in the proceedings. The eruption has cleared up completely on two occasions with gold and ultraviolet therapy. In each instance recurrence has followed neglect to carry out general measures. I believe sarcoid is of tuberculous origin. An article by Beinhauer and Mellon showed the circle with all types of tubercle bacilli from the filtrable virus through Much's granules to non-acid-fast and acid-fast form; as a matter of fact, they

have cultured some atypical tubercle bacilli from sarcoid lesions. At the University of Chicago Clinics atypical organisms were cultured from a patient who had subcutaneous tuberculids. I think the response to gold is a point in favor of the tuberculous origin. This patient so far has no sign of tuberculosis or generalized sarcoidosis, with the exception of calcification of some lymph nodes.

NOTE.—A subsequent tuberculin test with purified protein derivative in a dilution corresponding to 1 : 250 showed a strongly positive reaction. This is unusual in ordinary sarcoidosis.

DR. OLIVER S. ORMSBY: When I saw this patient in 1936 she had a moderate amount of trouble. In the three years between 1936 and 1939 she had much arsenic by mouth and by injection, also injections of gold sodium thiosulfate, administration of vitamins and other measures that should help were instituted. When she was presented in 1939 there was much improvement; even the cystic lesion in the bone had improved. For the next two years little change occurred. In 1941 she had a severe exacerbation. A new set of glands became involved, and there was more osseous involvement. The plaques became active, and many new lesions developed. About that time it was suggested that a preparation of chaulmoogra oil which was being of service in treatment of tuberculous conditions be used. I instituted that treatment last December. She has had thirty-seven injections, and the result is remarkable. The plaques have all undergone involution and show no signs of progression. A cystic lesion of the bone on the thumb has absorbed, and altogether the patient has made great improvement.

Amyloidosis Cutis. Presented by DR. J. H. MITCHELL and (by invitation) DR. F. W. HETREED.

P. M., a white man aged 49, of Italian descent, was entirely free of symptoms until one year ago, when he noticed a gradual increase in pigmentation of both legs. They were rough to the touch, and the itching became intense. Both pigmentation and itching became more aggravated until about six weeks ago, when he was first seen at the clinic.

On examination both lower extremities from just below the knees to the ankles show a diffuse brownish pigmentation with some small areas of atrophy. On the anterior and lateral surfaces are pinhead-sized, flat-topped, shiny, irregular papules. On the upper medial surface of the left leg a subcutaneous injection of congo red was made two days ago.

Histologic examination showed the deposit of amyloid stained with methyl violet.

DISCUSSION

DR. FRANCIS W. LYNCH, St. Paul: I doubt whether amyloid cutis is as rare as is indicated by the sparsity of clinical presentations. Its diagnosis requires the degree of alertness exhibited by the presenters of this case. An obstacle to more frequent diagnosis is the difficulty met in attempts at staining the amyloid; a negative staining reaction does not exclude the diagnosis, though a positive reaction is required for proof of the diagnosis. In individual cases, the amyloid material may react differently to the standard stains, and several attempts must be made before a tentative clinical diagnosis may be discarded.

DR. UDO J. WILE, Ann Arbor, Mich.: I wonder whether in every case of localized amyloidosis there would necessarily be shown the reaction to congo red. The color reaction is pale, but histologically the section showed localized amyloid changes.

DR. J. H. MITCHELL: Clinically those lesions are, I should think, easily overlooked. Dr. Hetreed made the diagnosis and made the injection into the lesion before I saw the patient. The lesions are somewhat less pronounced than they were. Clinically the demonstration of the staining with congo red is all that Dr. Nomland would ask for.

Arthropathic Pustular Psoriasis. Presented by DR. M. H. EBERT and (by invitation) DR. M. OTSUKA.

S. D., a white man aged 23, presents a fairly generalized eruption associated with polyarthritis. His first attack occurred three years ago. This was a disabling polyarthritis associated with cutaneous lesions of the same type as at present. That attack lasted three months. He was completely free until four months ago, when he had an acute exacerbation of the polyarthritis and a general eruption. When he was first seen at Cook County Hospital, six weeks ago, the eruption consisted of discrete psoriasiform plaques which were exudative and inflammatory. In many of the lesions there were numerous lakes of pus 1 to 3 mm. in diameter. Smears taken from this pus stained with Gram stain revealed no organisms. His nails were affected, particularly the toe nails. With the administration of salicylate his arthritis has practically cleared and his cutaneous lesions have become less inflammatory and are in the process of involution. He gives a history of a gonorrheal urethritis four years ago which was present for several months. He knows of no complications.

At present there are large well defined dull red plaques occupying the anterior surface of each leg and extending onto the calves and the dorsa of the feet. On the feet a few pinhead-sized pustules are still present at the margins of the plaques. Large nummular plaques of the same type occur on the thighs, buttocks, sacrum and abdomen and on the extensor surfaces of the arms. These are clearing centrally. When he was first seen, there was heavy keratotic scaling of the soles, but this has nearly absorbed. There is still considerable subungual keratosis of the toe nails, with some dystrophy. Large scaling patches are present in the scalp.

Repeated examinations of strippings from the prostate and the seminal vesicles did not reveal gonococci. The gonorrheal complement fixation test of the blood serum gave a negative result. Urinalysis and cultures of the blood failed to reveal gonococci. The blood chemistry was normal. The hemoglobin content at the last examination was 67 per cent, and there were 3,870,000 erythrocytes and 5,400 leukocytes, with a normal differential count. A roentgenogram of the chest was normal.

A histologic section from a pustular plaque on the leg showed a well defined lesion, characterized by decided changes in the epidermis. Between the lamellas of the thickened stratum corneum there were large lenticular collections of polymorphonuclear leukocytes. These cells stained well and were not degenerated. There was in addition, a patchy parakeratosis of the stratum corneum. There was acanthosis of the rete pegs, with compensatory elongation of the papillae, which extended almost to the stratum granulosum. In small areas the edema of the upper rete was greater and there was active migration of polymorphonuclear leukocytes, which accumulated under the stratum corneum.

DISCUSSION

DR. EDWARD A. OLIVER: I should like to ask Dr. Ebert if he used any vitamin D in treating this patient.

DR. S. W. BECKER: A note in the history stated that a section was removed from a pustular lesion. The section showed a great deal of material consisting of polymorphonuclear leukocytes in the scale, but I saw none at all in the epidermis or the dermis. I should like to ask Dr. Ebert whether he thinks it is necessary to find these collections in the living portion of the skin before a diagnosis of pustular psoriasis can be made. Clinically I should call it an exudative psoriasis of the arthropathic variety.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic changes, I believe, fit in with a pustular psoriasis, even though there is relatively little infiltrate in the cutis or evidence of migration of leukocytes through the epidermis. There were no cocci in the stratum corneum, which, in my experience, are always present in dermatitis repens or acrodermatitis continua. In regard to arthritis in psoriasis, when arthritis is associated with psoriasis, especially the so-called psoriatic arthritis, then the psoriasis is usually more severe than in cases of psoriasis without arthritis. Whereas psoriatic arthritis usually starts in the terminal phalanges, I have seen a good many persons with polyarthritis of varying-sized joints. This may assume destructive forms. As a rule, psoriatic arthritis responds much more quickly to a psoriatic regimen, with crude coal tar, ultraviolet irradiation and supplemental physical therapy, than do other nonpsoriatic forms of polyarthritis to physical therapy.

DR. J. H. MITCHELL: I thought the lesions on the plantar surfaces were typical of pustular psoriasis. The point I want to bring out is that at one of the spring meetings this same case was discussed, and somebody made the statement that involvement of the nails is not seen in arthropathic psoriasis. I recall a patient whom I saw in Dr. Senear's clinic at the meeting of the Academy with typical arthritic pustular psoriasis, particularly of the thenar eminences, involvement of the nails, classic pitting and other changes. This patient had numerous changes in the finger nails and only a few in the toe nails.

DR. M. H. EBERT: At the Cook County Hospital I have had opportunity to see two types of arthropathic psoriasis, one in which the patients are bedridden with polyarthritis and have psoriasis which seems to be of an atrophic variety. From the appearance of the cutaneous lesions one can usually state that there is an associated arthritis. This type lasts for years and does not respond to therapy. Then one sees this other type, which Dr. Becker described as the exfoliative type, in which the polyarthritis and the psoriasis both respond to treatment but tend to recur. In the second type there are many points of resemblance to keratosis blennorrhagica both clinically and pathologically. We reviewed the history of this patient and found that he had gonorrheal urethritis a year before the onset of his first symptoms. That was cleared up, and repeated study in our laboratory and in other laboratories of strippings of the prostate and seminal vesicles have since failed to indicate the presence of cocci; so it is hard to relate the urethritis with the present syndrome. However, he had other symptoms suggesting gonorrheal keratosis and severe involvement of the nails. When he was first seen, there were definite pustules in many of the lesions. They were pinhead-

sized lakes of pus. The first thing we did when examining this patient was to puncture these pustules and make smears, which were stained with the Gram stain. There were no gram-negative cocci or other organisms.

As far as the histologic structure is concerned, I have had the opportunity to study the slides in some detail. The most striking feature is the accumulation of polymorphonuclear leukocytes beneath the stratum corneum and between its lamellas. There was considerable migration of leukocytes through the edematous rete. Civatte has pointed out that in pustular psoriasis the polymorphonuclear leukocytes are well preserved and in the microabscesses they shrink up as they are exfoliated but do not disintegrate.

There are other factors that might cause pustules on the skin. This man was given iodides. One has to rule out pustules from ingestion of a drug.

I think this is a bona fide case of pustular psoriasis with polyarthritis.

Perifolliculitis Capitis Abscendens et Suffodiens. Presented by Dr. David V. Omens and (by invitations) Dr. Harold Omens, Dr. Masashi Otsuka and Dr. Willard Michelson.

W. S., a Negro laborer aged 43, presents an eruption involving the scalp of two years' duration. On the back and sides of the head are numerous variable-sized nodular masses which enlarge and coalesce. On palpation these masses are soft and contain numerous openings which exude a seropurulent material. This eruption, which has responded to treatment, started on the back of the head and has spread up to and involves the top of the head. The patient was seen in the clinic for the first time yesterday.

DISCUSSION

Dr. M. R. Caro: This patient was under care at the Mandel Clinic of Michael Reese Hospital about two years ago. The lesions of the scalp at that time were only a part of a generalized deep pustular eruption. He had many draining sinuses in the groins, in the axillas and on the buttocks. Treatment with sulfanilamide was started, and within two months he was improved sufficiently to go back to work.

Dr. Carl W. Laymon, Minneapolis: Dr. Caro's remarks agree with the ideas of Dr. Louis Brunsting, who believes that pyodermas of this type are linked with a disorder of the apocrine glands.

Basal Cell Epithelioma with Pigment, Secondary to Pigmented Nevus. Presented by Dr. R. B. Coomber (by invitation) for Dr. Clark W. Finnerud.

C. B. O., a railroad conductor aged 55, was first seen on Feb. 16, 1942, because of a lesion of the skin of the sternal region of fifty years' duration. He stated that the lesion had existed as a pea-sized nodule, which he considered a brown pigmented mole, until the last three years, during which time it had increased greatly in size. There were no subjective symptoms. Dr. James H. Mitchell saw the patient in consultation and agreed with the clinical diagnosis.

At the time of the first visit there existed a mottled light and dark brown, moderately elevated plaque, 4 by 5 cm., the center of which contained a pea-sized rather firm nodule; the plaque had a rolled border. No biopsy was performed. Roentgen rays (12,600 r) were administered in ten treatments, with the result as demonstrated today.

DISCUSSION

Dr. S. W. Becker: As the case was presented today, it is a typical picture of pigmented basal cell epithelioma after treatment. There is a great deal of melanin still present in histiocytes. I doubt whether the tumor originated from a nevus. I do not believe a microscopic section was made of the original brown lesion. All dermatologists have seen in routine sections nevi closely associated with basal cell epithelioma. I doubt very much whether there is any real connection between the two.

Necrobiosis Lipoidica Diabeticorum. Presented by Dr. E. A. Oliver and (by invitation) Dr. S. M. Bluefarb.

L. D., a waitress aged 30, was first admitted to Northwestern University Medical Clinics on Feb. 13, 1942, with the history of polyuria, polydipsia and increase of appetite for the preceding one and one-half years. Examination on that date revealed that she was suffering from acidosis, and hospitalization was advised. Her blood pressure was 118 systolic and 74 diastolic. Examination of the urine revealed sugar (4 plus), acetone (4 plus) and diacetic acid (4 plus). The sugar content of the blood was 333 mg. per hundred cubic centimeters; the cholesterol content, 393 mg., and the carbon dioxide–combining power, 51.2 volumes per cent. The patient was hospitalized for ten days and given the following diet: carbohydrates

150 Gm., proteins 65 Gm. and fats 70 Gm., with 20 units of insulin. She was referred to the dermatologic department on Oct. 12, 1942 because of the dermatitis on her legs.

Examination revealed three plaques on the right leg, two on the left leg and two on the left forearm and hand ranging from the size of a dime to that of a half-dollar. The plaques are well defined and are yellowish in the center and at the border. The surface has a glazed appearance, with beginning atrophy in the center. The present laboratory values are: cholesterol, 245 mg. per hundred cubic centimeters; erythrocytes, 4,860,000; hemoglobin content, 15.4 per cent and leukocytes, 7,900. Although the diabetes is under control, new plaques are being formed. The most recent lesion appeared two months ago.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: Looking at this patient's hands alone did not suggest in any way to me the diagnosis, which is so evident when one sees the lesion on the leg. This is the first case that I have observed in which necrobiosis occurred on an upper extremity.

DR. JOHN F. MADDEN, St. Paul: It is interesting to note that the lesions on the hand followed injury. There seems to be disagreement as to whether or not necrobiosis lipoidica diabeticorum follows trauma.

DR. MAURICE OPPENHEIM (by invitation): This case of dermatitis atrophicans diabetica is typical. The difference between granuloma annulare and dermatitis atrophicans diabetica is great. Ellis confused these different clinical entities. They are neither clinically nor histologically alike, as Dr. Montgomery said in Cleveland, and must be strictly separated.

DR. EDWARD A. OLIVER: I should like to ask Dr. Michelson how often he has seen lesions on the arms and hands.

DR. H. E. MICHELSON, Minneapolis: Dr. Laymon and I searched the literature on the subject and found one or two Italian reports in which lesions were noted on the arms.

DR. THEODORE CORNBLEET: I saw an excellent example of necrobiosis lipoidica on the hands in Dr. Senear's clinic.

DR. S. M. BLUEFARB (by invitation): This patient has been controlled by diet and 10 units of insulin a day.

Trichotillomania. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. HENRY C. SCHORR.

I. D., a white woman aged 45, shows patchy, incomplete alopecia of the scalp, with some erythema. There are no scars. The eyebrows are mostly devoid of hairs, and many of the lashes are missing. The disease has been present for two years. The patient admits pulling her hair in response to formications starting on the chest and arms and radiating to the scalp.

DISCUSSION

DR. THEODORE CORNBLEET: I think trichotillomania is a form of compulsion neurosis which manifests itself in various fields of medicine and which dermatologists see in several variations, such as trichotillomania and neurotic excoriations.

UDO J. WILE, M.D., *President*

MICHAEL H. EBERT, M.D., *Secretary*

Nov. 18, 1942

A Case for Diagnosis. Presented by DR. DAVID V. OMENS and (by invitation) DR. HAROLD D. OMENS.

L. M., a Negro girl aged 14 months, presents a patchy depigmentation of the skin on the left side of the chest which has been present for five weeks. The patches vary in size from that of a finger nail to that of a small coin and occur along the distribution of the nerve, not unlike the lesions of herpes zoster. There is no alteration of the skin except for the pigmentation.

No laboratory examinations have been made.

DISCUSSION

DR. EDWARD A. OLIVER: When I first saw the child, I thought of the depigmentation following herpes zoster, but on questioning the mother I learned that she had never noted a

vesicular eruption at any time on the side of the child's chest. In Negroes depigmentation often develops after an inflammatory lesion, but if the history is correct and there never was a zoster eruption I do not know what could have produced this depigmentation.

DR. HERBERT RATTNER: There is also the possibility in this case that the child may have ingested arsenic. Both zosteriform eruptions and hyperpigmentations occasionally follow ingestion of arsenic.

DR. D. V. OMENS: The reason I presented the case was that I thought perhaps the disease was herpes zoster with absence of zoster lesions, an unusual type.

DR. S. ROTHMAN (by invitation): Dr. Howard Fox presented a completely analogous case (ARCH. DERMAT. & SYPH. **7**:260 [Feb.] 1923). In it the lesions occurred in an adult Negro with no history of preceding zoster eruption.

DR. UDO J. WILE, Ann Arbor, Mich.: Can any one say whether depigmentation follows zoster in the Negro race? In the white race zoster is followed by hyperpigmentation.

DR. OLIVER S. ORMSBY: It is common in Negroes, much more so than in white persons.

DR. UDO J. WILE: There are abortive forms of zoster that occur without pain and with urticarial lesions. My impression of zoster in young children and in persons in the extremes of life is that it is very serious. It seems to be odd that a child should have zoster as a manifestation of disease without the mother's having noticed it or the child's having complained of it.

An Unusual Form of Naevus Pigmentosus. Presented by DR. S. BECKER.

R. T., a healthy, active boy aged 2½ years, first manifested hyperpigmented macules on various parts of the body at 8 months of age. The lesions slowly increased in number, but no new ones have appeared during the past six months. During the summer the child's skin between the lesions burns when exposed to the sun. The lesions themselves become somewhat paler during the summer. The mother states that the stratum corneum which is rubbed off after bathing is brown.

On various parts of the body, including the genital region and extending onto the median surface of the thighs, in both axillas and on the posterior portion of the neck, the dorsal aspect of both ankles, the right hand and fingers and other locations, are macules, light to dark brown. The shape is irregular, and the size varies up to several centimeters. The surface is slightly velvety, a condition suggesting that seen in acanthosis nigricans.

Histologic examination of a section removed from the dorsal surface of the ankle showed a thickened stratum corneum and thickened stratum granulosum. The epidermis was of approximately normal thickness and contained considerable pigment, especially in the basal portion. The papillae and the subpapillary layers of the epidermis showed a moderate number of chromatophores containing a brown pigment.

A section prepared by the berlin blue method showed no iron. Sections treated with silver nitrate showed pronounced pigmentation, most distinct in the basal layer. The stratum corneum, however, contained much pigment in the compressed keratinized cells. The basal layer was so deeply pigmented that it was difficult to identify individual cells. There appeared to be an excess number of melanoblasts located at the epidermodermal junction sending branches into the epidermis. The palisade basal cells showed prominent nuclear caps at the distal poles. Melanin was seen in decreasing amount toward the stratum corneum, where it appeared to be present in larger quantity because of the compression of the cells. There were no groups of cells, either in the epidermis or in the dermis, which could be designated as nevus cells, and no groups of pigmented cells were being carried to the surface, as is seen in lentigo maligna. The process may be interpreted as melanosis resulting from deposition of an abnormally large number of melanoblasts in the involved regions, at the junction of the epidermis and dermis.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I felt that some of the lesions looked much like those of the juvenile form of acanthosis nigricans. I was particularly impressed with the fact that there is some degree of acanthosis present in the lesions on the neck as well as in some around the genitalia. The progressive nature of the disease would seem also to lend color to that possibility. If this is acanthosis nigricans of juvenile type, I do not think any one could take issue with the diagnosis of pigmented nevus, because this is in a sense what the juvenile form is.

DR. OLIVER S. ORMSBY: I should like to corroborate Dr. Wile's discussion. Acanthosis nigricans was my first impression, but when I saw the lesions on the lower part of the body I was not certain. I should think that histologic examination would identify the disease.

DR. S. W. BECKER: I had the same impression when I first saw the boy. The first lesion I saw was on the back of the neck, and I thought that it was a lesion of acanthosis nigricans. The farther down I got the less certain I was until I saw the genital hyperpigmentation. It is a brown pigmentation, more nearly the color seen in nevi. The lesions also felt a little infiltrated, like those of acanthosis nigricans. In the sections there is distinct hyperkeratosis; the specimen was removed from the dorsal surface of the foot where the skin is a little thick. The predominant change is not an overgrowth of papillae as seen in acanthosis nigricans. I believe there are more than the normal number of melanoblasts located in these areas. The child has not acquired any new lesions for six months.

Annular Purpura. Presented (by invitation) by DR. STEPHEN ROTHMAN.

A woman, aged 32, switchboard operator and housewife, first noticed erythematous and pruritic patches on the leg three to four years ago. Since that time the eruption has appeared at irregular intervals on her legs and thighs. For two years she has felt stiffness and pain in the legs and joints. On the legs and thighs hemorrhagic lesions have developed, varying in size from that of a pinpoint to that of a nickel. The larger ones show a pale center and a dark red ring 1 mm. in diameter. In a few spots telangiectases are seen. Some spots are purely purpuric.

The Wassermann and Kahn reactions were negative. The count and differential count, platelet count, bleeding and clotting time and prothrombin values, were normal. The urine was normal on examination. The basal metabolic rate was —2 per cent. The response to the regular tourniquet (Rumpel-Leede) test was normal. At the sites of pressure of the garters, however, localized hemorrhages were observed. The diagnosis of hydropic arthritis was made in the arthritis clinic. The fasting value for ascorbic acid in the blood was 0.1 mg. per hundred cubic centimeters. After administration of ascorbic acid it was raised to 0.6 mg. per hundred cubic centimeters, but this did not influence the tendency to hemorrhage.

Histologic section showed mild perivascular infiltrate.

DISCUSSION

DR. HARRY R. FOERSTER, Milwaukee: My impression is that the annular lesions are probably accidental rather than significant of Majocchi's disease. I am of the opinion that this is probably purpura simplex secondary to whatever has caused the arthritis.

DR. THEODORE CORNBLEET: Dr. Rothman said that a determination of vitamin C had been made and that the level was rather low. Apparently he felt that the vitamin C probably had nothing to do with these lesions, and probably he is right. By the administration of vitamin C the blood level was raised, though how much and in what time was not stated. Perhaps more time should be allowed to permit the tissues to become more saturated.

DR. M. J. REUTER, Milwaukee: I believe that the vitamin C content of the blood has to go down to unmeasurable amounts before clinical purpura appears.

DR. S. ROTHMAN (by invitation): I fully agree that this is not a case of Majocchi's disease. In contrast to Majocchi's disease, the individual lesions in this case start with inflammatory signs. In addition, Majocchi's disease is not associated with arthritis. It is to be noted that in spite of the low initial values for ascorbic acid the hemorrhages have not been checked by the administration of ascorbic acid, although the blood level has been considerably raised. The case has been presented to show that the presence of a few annular lesions and telangiectases is not sufficient to establish a diagnosis of Majocchi's disease. In spite of the better knowledge of hemorrhagic diseases achieved through hematologic and vitamin research, the different clinical forms of purpura are still not clearly understood, and a reasonable classification is still not possible.

Solar Urticaria. Presented (by invitation) by DR. S. ROTHMAN and DR. C. L. SPURR.

This 39 year old housewife was never chronically ill until February 1942, ten months ago, when she noticed that each time she went outdoors into daylight pruritus, diffuse erythema and urticaria developed on the exposed portions of her body. This occurred repeatedly on clear and on cloudy days but never after sunset.

Physical examination did not reveal any abnormalities. The Wassermann and Kahn reactions were negative. Examination of the blood revealed: erythrocytes, 4,720,000; hemoglobin content, 14.9 Gm., and leukocytes, 6,900, with polymorphonuclears 57 per cent, large lymphocytes 2 per cent, small lymphocytes 31 per cent, monocytes 8 per cent, eosinophils 1 per cent and basophils 1 per cent. The sedimentation rate was accelerated (36 mm. per hour). Estimations of blood chemistry yielded normal results (uric acid, urea nitrogen, cholesterol, cholesterol esters, plasma proteins, dextrose, sodium, potassium, carbon dioxide, p_H and chlorides).

Hepatic function was normal by hippuric acid and colloidal gold tests. Routine examinations of urine and stools gave normal results.

A search was made for porphyrins in the urine. The first twenty-four hour specimen contained large amounts of a porphyrin showing a characteristic absorption spectrum with a sharp peak at 4,000 angstrom units. One later specimen of urine showed traces of porphyrin, but the following specimens were free of this substance.

Irradiation with a mercury vapor lamp and a carbon arc lamp with doses far below the erythema dose causes an immediate urticarial reaction in this patient. The urticaria is sharply limited to the area of exposure. It is surrounded by an irregularly shaped extensive red flare. This reaction persists for three to six hours and then gradually fades. Experiments with Corning filters have shown that the range of sensitivity to light is between the wavelengths of 3,300 to 3,500 angstrom units. This is a region in the long wave ultraviolet spectrum which is outside of the range of the "sunburn rays" and which to date has not been found to cause solar urticaria. In most published cases of solar urticaria, the patient was found to be sensitive to blue and violet (4,000 to 5,000 angstrom units). No porphyrinuria has been reported in cases of solar urticaria as yet. The causative role of porphyrin in this case is not established, because its absorption spectrum differs considerably from the range of the patient's sensitivity. At the present time studies are being carried out by projection of monochromatic light to the skin, in order to obtain a more accurate spectral sensitivity curve.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: I had occasion to observe a few cases of urticaria from sunlight, and I have every reason to believe that the sensitivity to the sun's rays is to wavelengths somewhere in the blue and blue-violet (longer) rays. In my experience these subjects have two features that Dr. Rothman has not pointed out. They all have dermographia, and this little girl had it. The second feature is they have a great sensitivity to histamine. A small amount of histamine injected subcutaneously will give rise to a histamine flush and a general histamine reaction. It is my opinion that these physical urticarias are produced by the long rays of light calling forth a histamine reaction which manifests itself on the skin by the formation of wheals. I do not believe the secretion of hematoporphyrin is of any importance in this type of urticaria.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to ask Dr. Nomland whether sensitivity to sunlight or sensitivity of this type to food would not be extremely unusual after the age of 36 years.

DR. RUBEN NOMLAND: I had 1 case in which a mother and daughter had it. The mother had urticaria from sunlight, and the daughter had dermographia only.

DR. OLIVER S. ORMSBY: Several years ago I presented a patient, a man aged about 40 years, who was subject to a physical allergy. He reacted with an urticarial eruption when exposed to the sun's rays. Immediately preceding the meeting he was exposed to rays from a mercurial vapor lamp which produced the eruption. At this time time Duke was making his studies on physical allergy, which included heat, cold and light.

DR. RUBEN NOMLAND: In addition, in some of these persons histamine flush of the face and histamine-like headaches develop spontaneously after they have had a severe attack of urticaria from exposure to sunlight.

DR. HARRY R. FOERSTER, Milwaukee: I recently observed solar urticaria in a woman 40 years of age, in whose case wheals were provoked not only by minimal exposures to sunlight but by ultraviolet rays under 3,500 angstrom units in length and in a dosage insufficient to provoke ultraviolet radiation erythema in normal skin. I mention that because Dr. Rothman speaks of the rarity of solar urticaria caused by rays of such short wavelengths. It is usually caused by wavelengths of visible light, approximately 5,000 angstrom units. I agree with Dr. Nomland's statement that porphyrinuria is of no significance in solar urticaria. Usually, as in this case, with porphyrinuria, the porphyrin activates light of different wavelengths than that which produces the cutaneous lesions. The finding of porphyrinuria is therefore probably coincidental rather than of etiologic significance.

DR. UDO J. WILE: Probably there are different types of solar urticaria. There are, for example, patients who burn easily, patients who after sunburn may have lupus erythematosus and others who react fairly quickly to solar energy and yet acquire only an urticaria. I daresay that except for the uncomfortable state produced such patients, except those who are subject to lupus erythematosus, are not in serious danger from exposure to sunlight or ultraviolet rays.

DR. RUBEN NOMLAND: I think this is a special type of solar sensitivity which is unrelated to any disturbance of porphyrin metabolism.

DR. S. ROTHMAN (by invitation): I agree with Dr. Nomland that the last link in the chain of events in solar urticaria is the liberation of H substance, as it is in all kinds of urticaria. However, the basic conditions are highly specific. There is a sensitization of the skin to a narrow range of the spectrum. As a result of this sensitization, the cells are damaged by the absorption of the corresponding rays. Liberation of H substance is a consequence of the damage to the cells. The sensitization must be due to a substance in the skin with an absorption spectrum which is similar to the urticariogenic action spectrum. This substance in the case presented is certainly not a porphyrin: first, because of the difference between action and absorption spectrums, and, second, because the sensitivity to light has persisted, although after the initial two porphyrin-containing specimens of urine numerous repeated tests did not reveal any porphyrin either in the urine or in the plasma.

It is true that since Duke first reported on solar urticaria, the majority of subjects were found to be sensitive to blue and violet. However, as mentioned in H. Blum's excellent monograph, there are a few cases of sensitivity to ultraviolet rays. Our filter experiments leave no doubt that the sensitivity in the case presented lies in the so-called long wave ultraviolet range.

There is no urticarial response to heat and cold stimuli. We have also been unable to elicit definite factitial urticaria in response to mechanical stimuli.

Addendum.—The patient shows normal urticarial response to histamine but an exaggerated red flare around the histamine wheal. There is no urticarial response to intradermal injection of acetylcholine and no dermographia elevata.

A Case for Diagnosis. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. C. SCHORR and DR. D. COHEN.

W. M., a Negro aged 58, a stationary fireman by occupation, presents pruritic lesions on the right forearm, wrist and hand which have been present for two years. On the left side of the chest there is a large patch which is of one year's duration.

Two years ago, the patient noticed a "pimple" on the lower part of the right forearm. This original lesion enlarged until it attained its present size. The right hand is enlarged and edematous. Verrucous plateaus that are sharply outlined cover the dorsum and extend over the wrist and part of the forearm. There are no pustular insets, but pus exudes on manipulation and at the site of a wound made for removal of a biopsy specimen. A part of the lesion is covered by a scaly crust, removal of which uncovers a shallow ulcer. There is an odor of putrefaction. The lesion on the wall of the chest, about the size of a saucer, is of the same general nature, although there is no scarring or ulceration. Here, too, pus exudes when the superficial crusts are removed. The epitrochlear and axillary glands are enlarged on the affected side.

Histologic examination of sections from the right forearm and the left side showed the changes of tuberculosis.

DISCUSSION

DR. M. H. EBERT: When I saw the patient, the border suggested blastomycosis. The lesions on the skin were of the type of blastomycosis here presented, but so far as I have seen blastomycosis does not cause sepsis sufficient to bring about the lymphedema this man had unless there is much scarring plus secondary infection. I was inclined to accept the diagnosis of tuberculosis verrucosa cutis. If it is that disease, it is a vastly different type than I have ever seen. I have seen few cases in which the lesions were as extensive as this. In examining the section there were a mixed infiltrate with epithelioid cells and some giant cells, which is suggestive but not diagnostic of tuberculosis. After looking at the section I had a discussion with Dr. Benedek, and I shall give him an opportunity to continue this discussion in public.

DR. TIBOR BENEDEK (by invitation): This case was presented as one of tuberculosis verrucosa cutis without the necessary consideration of a rather complex differential diagnosis. In Europe I saw many patients with tuberculosis verrucosa cutis with small isolated patches on the face, fingers, forearms and toes and even large plaques covering the whole buttock, for instance. The older school of dermatologists made a difference between tuberculosis verrucosa cutis and lupus vulgaris verrucosus. Modern American and European literature, however, dropped this differentiation entirely.

As to the differential diagnosis in this case, two diseases have to be considered above all: (1) blastomycosis (Gilchrist) and (2) chromoblastomycosis. The extreme degree of wart formation, the progressive destruction of the affected tissues and the elephantiasis of the fingers and the hand of rather considerable volume might lead the investigator in the direction of chromoblastomycosis.

From the two sections of the same biopsy specimen one does not obtain any useful information; the other one is not typical for tuberculosis verrucosa either. The epidermis shows pseudoepitheliomatous proliferation, rather inconsistent with tuberculosis verrucosa cutis. Furthermore, there are too many foreign body giant cells beside exceptional giant cells of the Langhans type in a rather unspecific granulomatous infiltrate. Here again the foreign body giant cells direct the thought toward chromoblastomycosis, in which these cells are considered by most of the authorities as the outstanding feature of the pathologic changes.

In such a case as the one presented one biopsy is not enough. Several specimens are required from different points of the affected areas. Most of all, however, I missed a thorough cultural investigation. Both in blastomycosis and in chromoblastomycosis properly made smears, from closed pustules in the former and from scales of the verrucous excrescences in the latter, may show the causative organisms. In both instances the culture does not cause any particular difficulties. But for a final and unquestionable establishment of the diagnosis cultural proof of the presence or absence of the Koch bacillus is also necessary. If the authors will use Keil's method (Keil, E.: *Arch. f. Dermat. u. Syph.* **160**:160, 1930) for the culture of the Koch bacillus, they will easily succeed despite the colossal secondary infection. The search for the causative organism must be carried on in both directions with mycologic and bacteriologic methods, since the final decision as to the therapy and the whole prognosis are dependent on the results.

All in all, with regard to such an extraordinary condition as here presented, the superficial clinical impression and a single biopsy are certainly not enough to secure the acceptance of the suggested diagnosis of tuberculosis verrucosa cutis at face value.

DR. MAURICE DORNE: I examined this patient in August 1935, and at that time he was a fireman in the Congress Hotel. Lesions had developed on the forearm three years before, and he thought they might be from dust. The lesion was one-third to one-half the size it is now. Clinically the diagnosis at that time was tuberculosis verrucosa cutis.

DR. MAURICE OPPENHEIM (by invitation): I want to call attention to the fact that tuberculosis verrucosa cutis and lupus verrucosus cutis are two different forms of tuberculosis of the skin. The former is the necrogenic wart, and the latter is lupus vulgaris with hyperkeratosis. Tuberculosis verrucosa cutis, first described by Saltauf and Riehl as a special form of cutaneous tuberculosis, shows abscesses caused by secondary infection; the tubercle bacillus invades the skin from outside; it is an occupational disease of the skin occurring in physicians, in nurses, in persons working in laboratories and morgues, and in furriers, straw hat workers and others. I believe that the present patient is suffering from lupus verrucosus elephantiasticus. One can find such pictures in the old dermatologic atlases of von Hebra, Kaposi, Neumann and others. Similar lesions are also caused by leprosy, elephantiasis syphilitica and leprosa.

DR. M. R. CARO: There was a case presented before this society several years ago (Mitchell, J. H., and Scull, R. H.: Tuberculosis Verrucosa Cutis and Lupus Vulgaris, ARCH. DERMAT. & SYPH. **35**:332 [Feb.] 1937) that brought out a similar discussion. In that case there were two different types of lesions present, and it was pointed out that in a Negro tuberculosis of the skin differs greatly in its course from that in a white patient. In the present case I believe that the disease is tuberculosis verrucosa cutis.

DR. MAURICE DORNE: I called my office after I recognized the patient and found that several months after I examined this man he was seen by Dr. Zeisler, who made a diagnosis of lupus vulgaris verrucosa.

DR. THEODORE CORNBLEET: It seems to me the two possibilities are a deeper mycosis and tuberculosis. The deeper mycosis would most likely be either blastomycosis or chromoblastomycosis; their elimination will have to await further microscopic and cultural examinations. So far no suspicious organisms have been found.

As for tuberculosis, as others have stated, it can readily be imagined to be the proper diagnosis if elephantiasis were secondarily present. It is known that Negroes more often acquire excessive fibrosis and elephantiasis than do white persons. The more fruitful area for study would appear to be the one on the trunk, because there is no complication with elephantiasis.

Pemphigus Erythematosus. Presented by DR. S. J. ZAKON.

This patient was presented previously at the Oct. 15, 1941 meeting (ARCH. DERMAT. & SYPH. **45**:791 [April] as having pemphigus erythematosus (Senear-Usher). His illness began in May 1941 and since July 1941 he has been treated by acetarsone and is practically free of lesions. When use of acetarsone is discontinued, his symptoms tend to recur. He has

thus far ingested four hundred 0.25 Gm. tablets of acetarsone. His blood was examined on November 15 and showed a hemoglobin content of 13.9 Gm. and a cell count of erythrocytes 4,420,000, leukocytes 5,800, segmented neutrophils 62 per cent, small lymphocytes 32 per cent, large lymphocytes 2 per cent and monocytes 4 per cent. Urinalysis yielded essentially normal values.

DISCUSSION

DR. J. H. MITCHELL: I think it is well within the range of possibility that that diagnosis is correct.

DR. EDWARD A. OLIVER: Dr. Zakon presented this case a year or two ago, and he presented it today for the purpose of demonstrating the efficacy of his therapy with acetarsone. He has several patients with pemphigus and with pemphigus erythematosus whom he has treated with acetarsone. The results are interesting.

DR. UDO J. WILE, Ann Arbor, Mich.: I understand that when use of arsenic is discontinued the lesions tend to recur.

DR. MAURICE OPPENHEIM (by invitation): This case stresses the effect of treatment with acetarsone, which I introduced in 1926. The poor results in this treatment were caused by the mistake that the treatment was stopped too early or was interrupted, or the administration of the acetarsone was not correct. For instance, Kromayer treated with 600 and 800 tablets (each tablet 0.25 Gm.) and had excellent results. I advise use of acetarsone in the treatment of pemphigus, but one should never interrupt the treatment and should watch carefully that no complications of the arsenic-phenol treatment occur. If a complication appears, the treatment must be interrupted or reduced to a smaller dosage. I have had excellent results. The vesicles and bullae become smaller and less numerous, often turn to nodules and papules and finally disappear. In one of the next issues of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (**47**:40 [Jan.] 1943) an article in collaboration with Dr. Cohen will appear covering this treatment. I would make the suggestion that in every case of the pemphigus group a trial of prolonged treatment with acetarsone under careful observation should be made.

DR. UDO J. WILE: Do you feel that this substance has any advantage over other forms of arsenic?

DR. MAURICE OPPENHEIM: One does not get the same effect from solution of potassium arsenite, U. S. P. (Fowler's solution) or from asiatic pills or other arsenicals. It is the compound of arsenic with benzene, a pentavalent organic arsenic compound, which causes the good therapeutic results.

DR. OLIVER S. ORMSBY: For a matter of record, in February 1918 Dr. Mitchell and I showed a patient that had this disease. We presented the case for diagnosis, and several diagnoses were suggested. After observation we decided the disease was a benign type of pemphigus. That man was treated for several years and made a complete recovery. Within the past ten days we have seen him, and his cutaneous lesions have not recurred.

DR. S. J. ZAKON: I do not think that acetarsone is a "cure" for pemphigus, since this is probably a case of benign pemphigus. At the suggestion of Dr. Oliver I presented this patient again to show the good effect of acetarsone administered over a long period. He took four hundred tablets without any deleterious effects on the blood cells. I think it was Levaditi who said to give the medication for three days and to allow a three day rest period for excretion. The advantage of this drug over the inorganic solution of potassium arsenite is that it is a pentavalent organic compound—an arsonic acid—and has the ability to penetrate into the central nervous system.

Lupus Erythematosus of the Eyelids. Presented by DR. E. A. OLIVER and (by invitation) DR. S. M. BLUEFARB.

J. S., a white boy aged 12, first noticed the lesions on his eyelids about thirteen months ago. There are no subjective symptoms. The lesions are erythematous and covered with a silvery white scale. There is no atrophy or telangiectasia.

DISCUSSION

DR. HARRY M. HEDGE: The patient has had the disease for two years and shows at the present time no particular atrophy of the areas that I can see. There was a little atrophy over the external canthus but not as much as one would expect to see in lupus erythematosus present for two years. The scales are rather whiter than those of lupus erythematosus.

DR. F. E. SENEAR: It is always interesting to observe cases in which the distribution is one that is not ordinarily associated with the disease. We have had that experience in this society with lichen planus, and more recently in Minneapolis several cases of lichen planus of the eyelids have been described.

In answer to Dr. Hedge's comment, I have under observation at the present time a woman in the sixties whom Dr. Oliver saw with me. She has an involvement of the eyelids which appears to be purely erythematous but which was diagnosed some years ago by Dr. Pusey as lupus erythematosus. She was under his observation for two years. Neither of us could ever make out anything except an erythematous dermatitis. While she has been under observation, lesions have developed in the malar portion, where she has never had lesions previously. In spite of the fact that she has had five recurrent attacks, each one lasting for some months or years, and has responded to the usual treatment for lupus erythematosus, she shows no scarring. Changes that any dermatologist would recognize as lupus erythematosus are now developing. I do not think the lack of scarring is against the diagnosis.

DR. S. W. BECKER: The lesions on the eyelids did not look like lesions of lupus erythematosus. There was no follicular plugging. The section showed considerable change in the epidermis with not much in the dermis. While I do not believe one can establish the diagnosis of lupus erythematosus, I have nothing else to offer. The clinical and microscopic pictures are certainly atypical.

DR. M. H. EBERT: I should like to call attention to the fact that this child had on either side of the tongue a bright red area that was well demarcated, smooth and shiny. Dr. Becker and I discussed the case and thought the lesions were benign plaques. I cannot say that they were characteristic of lupus erythematosus, but I think it is part of the clinical picture in the case.

Lymphoblastoma (Mycosis Fungoides?). Presented by DR. E. E. STENHOUSE.

J. W., a janitor aged 56, was first examined on Sept. 29, 1942. About sixteen months ago he noticed a generalized pruritus. There were no cutaneous lesions until eight months ago, when small, erythematous, pruritic papules began to appear on the arms, increasing rapidly in size and spreading to other parts of the body.

The eruption at present consists of papules and tumors on the chest, back, extremities, face, scalp and neck varying in size from 0.5 to 1.5 cm. in diameter. The lesions are red, firm and elevated. The tumors are largest and most numerous on the face and neck. The pruritus is no longer intense.

Physical examination revealed a blood pressure of 164 systolic and 96 diastolic and a chronic nasal obstruction (which the patient had had for fifteen to sixteen years). The liver could barely be felt below the costal margin. The spleen was not enlarged. The glands were not greatly increased in size. The Wassermann and Kahn reactions of the blood were negative. The blood count on October 20 showed: hemoglobin content, 14.7 Gm.; erythrocytes, 4,430,000, and leukocytes, 5,900 per cubic millimeter, with a differential count of 72 per cent polymorphonuclear leukocytes, 1 per cent large lymphocytes, 17 per cent small lymphocytes, 4 per cent monocytes, 6 per cent eosinophils and no basophils and some stippling of the erythrocytes. The urine was normal. A urea clearance test of the urine gave results within normal limits. The uric acid level of the blood was 2.3 mg. per hundred cubic centimeters. The stools from a meat-free diet showed no blood. Nasal smears showed no Hansen bacilli. Sternal puncture on Oct. 15, 1942 showed a distribution of cells within normal limits. A roentgenogram of the chest was normal.

Examination in the ear, nose and throat clinic revealed a large nasal polyp, which was excised. Microscopic examination of the tissue showed no carcinomatous degeneration. A chronic suppurative otitis media on the right side was also noted. A specimen taken for biopsy from the neck showed hyperkeratosis and parakeratosis, with extension of keratotic material into the sweat pores and hair follicles. From the subpapillary portion of the dermis inward there was a perivascular and perifollicular massive infiltrate consisting of round cells, fibroblasts and a few epithelioid cells. The vascular endothelium was swollen. The follicular epithelium showed mild intercellular edema.

A section removed from a small lesion on the face showed the stratum corneum to be hyperkeratotic and parakeratotic about the follicular orifices only. Hyperkeratotic material extended into the orifice itself. About the follicles and blood vessels was a pronounced infiltrate consisting of round cells, fibroblasts and a few epithelioid cells. The vascular endothelium in the areas of infiltration was swollen. The follicular epithelium showed considerable intercellular edema.

DISCUSSION

DR. E. A. OLIVER: I am not at all certain about the diagnosis in this case. I do not believe the disease is mycosis fungoides. The diagnosis of lymphoblastoma would seem to be the best, though one must rule out leprosy and an aleukemic leukemia.

DR. UDO J. WILE, Ann Arbor, Mich.: It seems to me the lesions in the ear and on the forehead are exceptional in appearance and resemble those of leprosy. But the generalization of this lesion in a period of eight months and the extent of the lesion in the absence of anesthesia would rule leprosy out if the biopsy itself did not.

DR. S. ROTHMAN (by invitation): This patient had itching for several months before the eruption started. This does not suggest leprosy. I do not think that the distribution of the lesions on the forehead is atypical for lymphoblastoma.

DR. M. H. EBERT: Some of you will recall a case presented six months ago as one of lymphoblastoma. The patient was seen in one of the other services, and the presentation was rather hurriedly prepared. The dermatologists from Minneapolis and St. Paul were impressed with the fact that it was a case of leprosy because of the multiple nodules in the ears and the plaque on the face. The patient rapidly went downhill; the blood picture changed, and he died three weeks later of lymphatic leukemia. He had nodules that suggested leprosy much more than these do.

DR. UDO J. WILE: Time may establish the diagnosis for us. I think the rapidity of onset speaks for a blood-borne condition, that is, something in the nature of leukemia, perhaps a blood dyscrasia which is as yet not manifest in the blood itself. It must have been blood borne when these lesions were appearing. It is not anything like any lymphoblastoma I have seen before. I wonder if we may have Dr. Stenhouse report on the future progress and perhaps have repeated examinations of the blood made and observations of possible increase in size of the spleen.

DR. EVANGELINE STENHOUSE: The nasal smears have been made, and lepra bacilli were not found. A sternal puncture was also made, which showed no change in the bone marrow cells. I shall be glad to report subsequent developments.

DR. OLIVER S. ORMSBY: Leukemia appears the most likely diagnosis.

Tuberculosis Orificialis. Presented by DR. E. A. OLIVER.

The patient, a white man aged 55, from the Veteran's Hospital, entered the hospital on Dec. 15, 1941, at which time he stated that the swollen, infiltrated condition of his mouth was first noticed in the fall of 1941. In October of that year he first noted pain in the upper jaw. When he was seen in December 1941, the tissues covering the hard palate were swollen and infiltrated and had a rugous appearance; a similar appearance was noted in the tissues of the left buccal mucosa and to some extent in the tissues of the right buccal mucosa. The lower gum was swollen and irritated. His upper lip was edematous and infiltrated, and in the middle portion there was a rather deep ulcer, almost the size of a dime. He has tabes dorsalis and has been treated here and at the Mayo Clinic in 1925 for that disease.

Roentgenographic examination of his chest in June 1941 showed that the apexes were clear and that there was an increase in the bronchial markings, with interstitial fibrosis; a diagnosis of chronic bronchitis was made. Examination of the blood showed 5,100,000 erythrocytes, 8,900 leukocytes and a hemoglobin content of 90 per cent.

Histologic examination showed a tuberculous architecture.

DISCUSSION

DR. DAVID LIEBERTHAL: According to the clinical appearance of the oral lesions and the history, I believe that the patient had a syphilitic infection some years ago. The patient was examined thoroughly, and, though tubercle bacilli were found in some of the lesions, there is no justification to assume that one may have to deal here with two etiologic factors.

DR. F. E. SENEAR: I agree with the diagnosis of tuberculosis orificialis. I think the case is clinically typical.

DR. M. H. EBERT: I think this case is unusual in the sense that in the few cases of tuberculosis of the oral cavity of this type that I have seen the lesions occurred in persons who had active tuberculosis of the lungs or larynx. These people rapidly go downhill. I have never seen a lesion as extensive as this in a patient appearently in good health otherwise. I should like Dr. Oliver to tell us about the patient's general condition as far as tuberculosis is concerned.

DR. E. A. OLIVER: This case has been confusing for me for the same reason it has been to Dr. Ebert. In all the cases of tuberculosis of the buccal mucosa the lesions have occurred

in patients in the terminal stages of pulmonary or laryngeal tuberculosis. The pathologist at the Veteran's Hospital and Dr. Caro both say the sections are indicative of tuberculosis, yet the man is apparently in good health except that he has tabes dorsalis. Roentgenograms of his chest show no involvement of the apexes, but they show signs of an interstitial fibrosis.

When I first saw him, the ulcer on his lip was open and active and the verrucous element was much greater. Today the ulcer is almost healed. His treatment has consisted of localized and general ultraviolet irradiation.

A Case for Diagnosis. Presented (by invitation) by DR. S. ROTHMAN.

This 20 year old man was first seen in the University of Chicago Clinics in 1937, with the diagnosis of cirrhosis of the liver, splenomegaly of unknown origin (Banti syndrome?) and esophageal varices. Splenectomy and ligation of the left gastric veins was performed in January 1938. Because of recurrent attacks of hematemesis and tarry stools, a gastrostomy was performed in April 1939 to relieve esophageal varices.

The patient was readmitted to the hospital on Nov. 4, 1942 because of pain in the lower left quadrant of the abdomen and hematemesis. A test of hepatic function and biopsy of the liver revealed advanced damage of that organ.

Since the operations in 1938 and 1939 the patient has noticed that the left side of his abdomen is lighter than the right side.

The skin is slightly icteric. The skin of the abdomen shows hyperkeratosis, with discoloration of the thickened horny layer. There is a triangular light and completely smooth area on the left side of the abdomen with a sharp linear border exactly in the midline.

DISCUSSION

DR. S. W. BECKER: My impression of this patient was that the lighter area was probably not actually depigmented but that the rest of the surrounding area was scaly and keratotic. This keratotic material was brown. That same condition is seen in pellagra; in it there seems to be considerable hyperpigmentation, but if the hyperkeratotic stratum corneum is removed all this brown pigment comes off with it. The hyperkeratotic change might be on a nutritional basis.

DR. STEPHEN ROTHMAN (by invitation): I purposely did not use the term "depigmentation," because it is obvious that the primary change in this case is the hyperkeratosis, with discoloration of the thickened horny layer ("keratin color" of Unna). The triangular light area is not only normal as to pigmentation but is perfectly smooth as well. The dry skin with brownish scales in undernourished persons used to be known as pityriasis tabescentium. It would be interesting to find out to what degree this picture can be related to any particular vitamin deficiency. The noteworthy fact in the case presented is that a large area on the abdomen remains free of this sign of supposed nutritional deficiency. The free area is limited by a sharp line or border exactly in the midline. Thus, one has the impression that the severing of a cutaneous nerve at the time of operation may have been the cause of the absence of hyperkeratosis in this area.

Blastomycosis. Presented by DR. A. W. STILLIANS and DR. E. M. SMITH JR.

An Italian man, aged 55 years, has a scarring, somewhat active blastomycosis involving the lower part of the abdomen and the left leg. The eruption started on the middle of the left thigh (anterior) and has slowly spread. It is of about fifteen years' duration. The condition has been reported to his company only recently. He has been employed by the same company in making soap for more than twenty-five years.

Histologic examination clearly showed blastomycetes, even with low power microscopic field.

A Case for Diagnosis. Presented by DR. F. E. SENEAR.

This 66 year old white man first noticed an itching eruption involving the right axillary region five years ago. Gradually this extended to involve the whole surface of the body with the exception of the soles. The scalp, trunk and palms were especially involved. He states that new lesions, consisting of small "blisters" containing a thick yellow material, have continued to form constantly since the onset and that he has never been entirely free from the eruption since it first appeared.

He was first seen at the University of Illinois on Nov. 5, 1942. At that time there was a generalized eruption consisting of erythematous and pigmented patches on which were thick brownish crusts arranged in irregularly circinate and serpiginous manner. Scattered between the pigmented and crested areas were pinhead-sized pustules with erythematous bases. Many of these pustules contained gravity pus, which filled only the lower half of the lesion. The pustules were most profuse on the palms. Considerable itching was present.

Solution of potassium arsenite U. S. P. (Fowler's solution), 3 minims (0.18 cc.) three times a day, has been administered during the last ten days, with considerable improvement in the eruption.

A biopsy of a specimen from the back showed a tiny multilocular vesicle lying in the superficial part of the epidermis and containing within it many lymphocytes and polymorphonuclear leukocytes. The epidermis beneath the vesicle and on both sides showed considerable intracellular edema. The corium was edematous, and the papillae were wide and long. In the corium near the vesicle, the blood vessels were dilated and there was a perivascular infiltrate containing lymphocytes and many polymorphonuclear leukocytes and chromatophores.

DISCUSSION

DR. J. H. MITCHELL: I have the impression that that was an unusual dermatitis herpetiformis with pigmentation and vesicles.

DR. M. R. CARO: I think that histologically as well as clinically this is a puzzling case. The vesicles in the section from the back are superficial, much more so than are usually seen in dermatitis herpetiformis. On the other hand, they are also more superficial than are seen in any other condition that one would think of clinically.

DR. OLIVER S. ORMSBY: A positive diagnosis in this case is difficult. The flat pustules on the hand resemble those of pustular psoriasis. The other lesions are suggestive, but I do not think this man has pustular psoriasis. If one takes into consideration the duration of the disease, the pigmentation, the itching and the vesicular and pustular lesions, I think dermatitis herpetiformis will have to be strongly considered.

DR. UDO J. WILE, Ann Arbor, Mich.: It is interesting that this patient got considerable relief after the ingestion of solution of potassium arsenite, which seems to bear out Dr. Ormsby's suggestion that it is dermatitis herpetiformis.

DR. FRANCIS E. SENEAR: My colleagues and I, of course, found this a puzzling case. Our feeling is much like that expressed by Dr. Mitchell and Dr. Ormsby, that an atypical form of dermatitis herpetiformis is the most probable diagnosis. When we saw the patient first, the picture was quite different from that seen today. The lesions on the body were much more extensive. While he had many primary pustular lesions like those seen today, the larger lesions were much more extensive and were crust covered and some were rather gyrate and some serpiginous. Looking out for other possibilities, we thought of pustular psoriasis, which Dr. Ormsby has mentioned, because of the character of the palmar lesions. We also thought of the possibility of acrodermatitis continua. I looked up cases of generalized acrodermatitis continua and did not find any which corresponded to this one.

As to pustular psoriasis, I do not think the palmar lesions are those of psoriasis, largely on the ground that each of these pustules maintains its integrity; they are not groups of pustules situated on an inflammatory base, such as one sees in psoriasis of the palms.

The last thing we mentioned, and we did not consider it seriously, was the question of impetigo herpetiformis. The fact that this eruption occurs in a man makes that improbable. Secondly, so extensive a bullous eruption without any systemic manifestations would likewise be extremely improbable. In looking up some of the reports on impetigo herpetiformis, we were surprised to find that one photograph showed an eruption not as extensive as this but more or less in keeping with this picture. I was interested in seeing a report by Ayres, of Los Angeles, in the ARCHIVES in which he called attention to one observation which was definite in this case. In his case the diagnosis was not indisputable either, but the patient had bullous lesions which as they became larger became sacculated, with pus collecting in the dependent portion of the lesions. We have never seen primary pustular lesions in this case, as every lesion has been a bulla at the outset. An extensive group of fresh lesions has developed in the groin since yesterday. We debated whether to use the ingestion of potassium iodide or of solution of potassium arsenite as a therapeutic test. We followed the second choice, and the patient has shown improvement as far as the lesions are concerned, but while taking solution of potassium arsenite he acquired a fresh crop of lesions; hence the value of the solution can be questioned. I think a rare form of dermatitis herpetiformis is as close as one can come to the diagnosis.

A Case for Diagnosis (Localized Dermatitis Herpetiformis? Neurotic Excoriations?). Presented by DR. E. A. OLIVER and (by invitation) DR. S. M. BLUEFARB.

J. C., a man aged 63, stated that the lesions on his forehead started about eighteen months ago. The past history is essentially normal except for a history of syphilis about twenty-four years ago, with about two years of treatment at that time. At present the Wassermann reactions of the blood and spinal fluid are negative.

On the forehead there are crusted, excoriated lesions. The lesions are urticarial at the onset; no vesicular lesions have been seen. The patient was instructed to take a saturated solution of potassium iodide, 30 drops per day. There was an immediate flare-up of the lesions on the forehead. For the past two weeks the patient has been taking sulfapyridine, 20 grains (1.29 Gm.) per day, with great improvement clinically, and he states that the itching has practically ceased.

DISCUSSION

DR. M. H. EBERT: I am not as familiar with this case as the presenters, who have watched it for some time. Clinically it appeared to me as a case of neurotic excoriations. I examined the patient for hysterical anesthesia of the palate and found it to be complete. That is always present in cases of neurotic excoriations.

DR. S. ROTHMAN (by invitation): In a few places atrophic scars can be seen. I agree with Dr. Ebert that the lesions represent neurotic excoriations.

DR. HERBERT RATTNER: I have observed this man for some time, always with the diagnosis of neurotic excoriations. New lesions would appear despite the use of thick pastes, and then there was a definite exacerbation after the ingestion of potassium iodide. It was then suggested that the eruption might be localized dermatitis herpetiformis, and that is why the patient was brought here for discussion. It is still my opinion that the proper diagnosis in this case is neurotic excoriations.

DR. UDO J. WILE, Ann Arbor, Mich.: I would raise the question of the value of potassium iodide in establishing even a presumptive diagnosis, because almost any person can react to potassium iodide. Its value in differentiating between dermatitis herpetiformis and pemphigus has been negligible in my experience.

DR. J. H. MITCHELL: About two years ago a patient in the clinic who had long-standing dermatitis herpetiformis and who was employed in a large industrial plant cut his finger. Against his will, a nurse applied iodine. The resulting exacerbation was tremendous and led to an attempt on his part to collect damages.

Multiple Idiopathic Hemorrhagic Sarcoma. Presented by DR. F. E. SENEAR and (by invitation) DR. H. C. ROLL.

This man, aged 63, was first seen on April 21, 1939, in the department of dermatology of the University of Illinois. At that time, he presented an eruption of dusky red, hard papules, coin-sized infiltrated patches and tumor-like lesions on the trunk, upper and lower limbs, hands and feet. The lesions about the face and ears were hazelnut-sized globular tumefactions. The eruption had begun on the hands two or three months previously. Biopsy of a specimen from a tumor on an ear at this time showed the condition to be Kaposi's sarcoma. He was given a course of solution of potassium arsenite U. S. P. (Fowler's solution) and superficial roentgen therapy. On June 18, 1940, three months after cessation of treatment, the face was entirely clear and the remainder of the lesions showed considerable involution. At this time it was felt that further roentgen therapy should be withheld.

The patient was not seen again until Oct. 27, 1942, and he stated that he had recently noted new lesions and swelling of the ankles. At this time he shows small, bluish or purplish infiltrated lesions on the great toe. The extremities and trunk show old, infiltrated, brownish or purplish spots appearing much as they did when he was last seen two years ago.

Histologic examination of a new lesion from the left side of the chest showed a picture compatible with that of Kaposi's sarcoma.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich: I think the diagnosis was obvious when one examined the feet. I could not make a diagnosis of Kaposi's sarcoma, however, from any lesion on the body. There were some which did not appear to be more than scratch marks until one palpated them and noted that they were nodules. I have encountered a few cases of Kaposi's sarcoma in which there was rather general metastasis, but the metastases have always resembled the original nodules. From this standpoint I think this is the most unusual case presented today.

DR. MAURICE OPPENHEIM (by invitation): There is no doubt that the presented patient is suffering from Kaposi's sarcoma. My first impression when I saw the lesions on the body was syphilis. I have never seen such a generalized distribution involving the tongue and face.

DR. WILE: It must be relatively benign, for the man appears to be in fairly good health.

DR. OPPENHEIM: The course of this disease is often relatively benign. With arsenic and roentgen ray treatment patients can live fifteen to twenty years, and longer.

DR. H. M. HEDGE: The patient with Kaposi's sarcoma of the foot whom I presented some fourteen years ago had metastases on the trunk. There were four spots on the hip. He is still living and is working in a factory of a prominent manufacturer of ice cream.

DR. S. W. BECKER: I should like to question the use of the term "metastasis." My understanding of this disease is that these lesions originate in situ in many regions. When Kaposi's sarcoma becomes really malignant, true lymphatic metastasis occurs and the patient dies quickly.

DR. L. M. WIEDER, Milwaukee: How do you account for lesions appearing on the foot after they had appeared on the body?

DR. BECKER: Eventually a true sarcoma with true metastases develops. I think it is at first simply a multicentric tumor. I believe that these many lesions have originated in situ independent of the lesions elsewhere.

DR. FREDERICK R. SCHMIDT: Does not Dr. Becker mean that these are individual lesions produced in situ as a response of the reticuloendothelial system to a substance which is a toxin but which is not a virus? I think it is a tumor of reticuloendothelial cells.

DR. UDO J. WILE: I apologize for mentioning these as metastatic lesions, but they seemed so to me.

DR. F. E. SENEAR: I should like to comment on the picture when the patient was first seen several years ago. At that time there would have been no question clinically as to the diagnosis of multiple idiopathic sarcoma. When he came back ten days ago, I did not recognize the patient, and, seeing the lesions from a distance, I thought that they were dermatitis factitia because of the peculiar configuration. At that time the lesions were somewhat excoriated, which made them more suggestive of neurotic excoriations. With my limited experience with Kaposi's sarcoma, that type of lesion is unique.

Contact Dermatitis Due to a Sweat Shirt. Presented by DR. L. F. WEBER.

I first saw this man, aged 37 years, on November 6. An eruption appeared on his forearms and arms on October 30. About one week later the eruption involved the trunk, especially the sides. The eruption improved for several days, and then a more severe and extensive attack occurred. Originally, he had a diffuse redness of the forearms and arms. The trunk, especially on the sides, showed a diffuse redness, without vesicles. The axillary regions have not been involved. Today he shows considerable improvement, and in the last week his improvement has been rapid. Various patch tests were made with materials handled in his work and at home and with his wearing apparel. A positive reaction was obtained with the lining of a sweat shirt.

DISCUSSION

DR. S. W. BECKER: There were no vesicles that I could see; the skin was dry. The involved areas appeared somewhat like the dermatitis observed after the use of sulfur ointment. I questioned him about his work. He works in cutting oil, which he states has a sulfur base. Some of these oils are sulfonated. It seems they make a better emulsion than nonsulfonated oils. The eruption may be a sulfur dermatitis.

DR. RUBEN NOMLAND, Iowa City: I agree with the diagnosis. I think one can observe numerous cases of contact dermatitis from clothing in men. There is a certain element in the finish which can be present in cotton, silk and other material. I have seen persons with dermatitis caused by relatively inexpensive cotton drawers and less frequently by pajamas, most of which have been purchased from chain stores. The material gave a positive reaction on a patch test. It is a peculiar type of dermatitis, and when it is caused by drawers or pajamas there is an intense edema of the scrotum.

DR. UDO J. WILE, Ann Arbor, Mich.: I have seen an eruption caused by cheap cotton gloves purchased in a ten cent store.

DR. JAMES H. MITCHELL: Within the past week I had a patient with a similar eruption. The patient had a new sweat shirt and was doing intensive gymnastic exercises. The evidence is presumptive but not conclusive.

DR. L. F. WEBER: In answer to Dr. Becker, none of the patients I have had with dermatitis from wearing apparel have ever had a vesicular eruption. It has always been an erythematous eruption. This patient had the eruption confined to the forearms and arms, and the other parts of the body were clear. The hands were not involved. The reason the arms and forearms were involved first was that he had worn the sweat shirt over another shirt with short sleeves. The eruption spread, and later a dermatitis of the trunk developed. Later the sensitivity increased, and even though he wore a shirt underneath the sweat shirt he continued to have dermatitis. The sweat shirt has not been worn for the last eight days

and there has been 75 per cent improvement. With the positive reaction to the patch test I feel that this man has a dermatitis due to the lining of the sweat shirt. I had what I thought was a considerable experience with dermatitis due to wearing apparel, but I did not recognize it in this case for three days. I would not have recognized it then if a dermatitis on the arms had not developed.

DR. THEODORE CORNBLEET: I noticed that the axillas were perfectly clear of eruption, parts that would normally have plenty of dermatitis. I wonder if the relative alkalinity of the sweat in the axilla was a factor in preventing the eruption. Perhaps if the sweat shirt were washed thoroughly free of acid elements he would no longer be sensitive to it.

DR. L. F. WEBER: I think that one of the most important points that should be brought out is that the axillary regions are usually clear in a dermatitis from wearing apparel.

Sporotrichosis. Presented by DR. J. H. MITCHELL and (by invitation) DR. EDWIN M. MILLER.

This man first noticed a nontender infectious-like lesion in the distal end of the index finger about Aug. 15, 1942. He had been trimming hedge and thought at the time that it was infection caused by a sliver. There were two or three ulcerated areas but no drainage. No treatment was instituted. The patient states that his son has tame rabbits and that several of them died during the summer; the cause of their deaths is not known, although two or three of them had infections of the feet. The patient states that he cleaned some squirrels about September 1, two weeks after ulcerations developed on his finger.

After he had used paint remover the latter part of September, the terminal phalanx of the finger became swollen, red and tender. There was no drainage, and the condition subsided after four or five days. About October 5 the terminal phalanx of the finger again became swollen, after which red nontender nodules varying in size from that of a pea to that of a walnut developed on the dorsum of the hand, forearm and flexor surface of the arm. The doctor prescribed sulfathiazole, 15 grains (0.97 Gm.) every four hours, and warm moist dressings. In general, the patient felt below par. He was admitted to the hospital about Oct. 12, 1942 and given sulfapyridine and applications of warm moist dressings. The lesions subsided somewhat but did not drain. He was discharged about October 17, but his condition then became worse and he was readmitted to the hospital on November 3. He was given sulfathiazole, and warm moist dressings were applied, and the lesions subsided about 50 per cent after ten days. Examination showed erythrocytes 5,100,000, hemoglobin content 17 Gm. (106 per cent) and leukocytes 10,200. Two agglutination tests for tularemia gave negative reactions. The Mantoux reaction was negative with 0.1 cc. of old tuberculin diluted 1 : 100,000. The patient has had intermittent fever (his highest temperature 101.4 F.) but little axillary lymphadenopathy. Physical examination revealed otherwise normal conditions.

DISCUSSION

DR. H. R. FOERSTER, Milwaukee: I believe the indolence of the inflammation, its moderate severity and the absence of axillary adenitis, which is usually found in tularemia and is invariably absent in sporotrichosis, furnishes a clue to the diagnosis. I was much intrigued by the patient's admission that he had trimmed a barberry hedge and that his first intimation of trouble was what he felt to be a splinter in the tip of the index finger. He asked his wife to examine it, but no splinter was found. The index finger is a common site of primary sporotrichosis, especially when the lesion results from work in a florist's shop or tree nursery, and particularly when roses or shrubs have been handled. Prompt response to potassium iodide therapy would be confirmatory of the diagnosis of sporotrichosis. It is interesting that practically all the cases of sporotrichosis seen in this country are of this particular type, with lymphangitis on the flexor portion of the upper extremity and an associated chain of cutaneous or subcutaneous nodes. The type of sporotrichosis commonly encountered in Europe, with gummatous nodules of scattered distribution that resemble syphilis, is apparently rarely encountered here.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to ask Dr. Mitchell whether cultures are being grown from the exudate.

DR. H. M. HEDGE: I had an interesting case of sporotrichosis that was definitely diagnosed by cultures at the Evanston Hospital. The patient, a woman, had alleged that a ball that a child had lost rolled into the barberry shrubbery and that in recovering the ball for him she scratched the lower eyelid. The localization was peculiar, but we found the organisms.

DR. J. H. MITCHELL: I saw this patient on Saturday for the first time. He has been in the hospital in a surgical service, and up to the present sporotrichosis was not considered. He was treated with sulfathiazole. There have been exacerbations and remissions. One of

the interesting things was the bifurcation of the lymphatic lesion just below the elbow, one streak going up toward the biceps and the other on the back of the arm. The time has been too short for cultures to develop.

As regards Dr. Foerster's remarks about the type of sporotrichosis encountered in Europe, some of you may recall that I presented a case some years ago in which the eruption clinically resembled bromoderma, which was considered in the differential diagnosis. I made cultures at once. I tested the patient for bromine in the urine and went into the history of addiction to bromoseltzer. I promptly got a culture, which was of the jet black variety. I am inclined to believe that this is sporotrichosis, but the diagnosis has not been proved.

Colloid Degeneration of the Skin (Unilateral). Presented by DR. FREDERICK R. SCHMIDT.

F. P., a man aged 67 years, from the outpatient department of Grant Hospital, states that he has had severe itching and pain in the left side of his neck for the past three years. He has worked outdoors a good part of his life.

The skin of the back of the neck is dry, roughened and yellow and is marked off into rhomboidal areas by linear furrows. The skin of the left side of the neck and the anterior surface of the chest to about the third rib presents numerous hard, glistening, round, yellowish nodules, varying in size from that of a pinhead to that of a split pea. Excoriations, as if from scratching, are also present in this area.

The results of a neurologic examination were essentially normal except for hyperesthesia of the skin in this area to all modalities of sensations.

The results of routine laboratory tests were normal. The cholesterol content of the blood was 175 mg. per hundred cubic centimeters. Roentgenologic examination revealed a cluster of stippled concretions in the soft tissues in the region of the mandible on the left side, which were probably salivary calculi. The lower cervical vertebrae showed a moderate degree of osteoarthritis. The injection of a solution of congo red gave a negative reaction for amyloid.

A specimen removed from the left side of the neck showed the changes of colloid degeneration of the skin. The collagen throughout the section appeared for the most part swollen, homogenized and fragmented. Nuclei were only sparsely distributed throughout the cutis. The elastic fibers in the papillary body were in part short and broken up into small, swollen fragments. For the greater part they have been replaced by a homogeneous, blue-staining mass only sparsely dotted with pyknotic nuclei. A section removed from the right side of the neck did not show these changes.

DISCUSSION

DR. M. R. CARO: There is some degeneration in the fibers, but it is difficult to say whether the change is greater in the elastic fibers or in the collagen. The Weigert stain seems to show enough change in the elastic fibers to indicate that this is senile elastosis of the skin.

DR. MAURICE OPPENHEIM (by invitation): I agree with Dr. Schmidt and Dr. Caro. The patient has lesions which Jadassohn called cutis rhomboidalis nuchae. I should advise Dr. Schmidt to apply the methods of Unna to the sections, particularly the water blue method. The collagen bundles are converted to hyalin; the elastic fibers or the elastin is turned to elacin, then to collacin and to colloid as the end product. The colloid is the cause of the yellow color. But there is another opinion, first mentioned by Kreibich, that the yellow color is caused by a lipoid degeneration of the elastic fibers and of the collagen, as he found it in the skin of old people. What is most striking is the hypersensitiveness of the skin. If one touches it, the patient reacts violently; I cannot explain this. One observes a similar reaction in connection with nerves which are embedded in colloid, hyalin or scar tissue. Another significant feature in this case is the unilateral location.

DR. FREDERICK R. SCHMIDT: The neurologist has examined this man thoroughly and found no lesion of the central nervous system. I am inclined to agree with Dr. Oppenheim that the itching, which in this man is so intense that it interferes with sleep, is a local affair and due to impingement of the nerve endings in the skin. Dr. Caro mentioned that it is really elastic tissue which has degenerated, and I agree with this opinion. I chose the term colloid degeneration merely because in patients with these lesions there is always a degeneration of both collagen and elastica.

There is another fact that has intrigued me, namely, the presence of whitish glistening particles. There are about five or six of these little hard white particles composing the greater part of the nodules. In one respect they resemble changes seen in early calcification of the skin. It may be recalled that many of these early calcifications of the skin begin in the basal layer with bluish-staining degeneration of the elastica. About every other papilla was occupied by a bluish homogeneous mass. Similar pictures are observed in changes of colloidal cholesterol.

BROOKLYN DERMATOLOGICAL SOCIETY

M. M. ESTRIN, M.D., *President*

SEYMOUR H. SILVERS, M.D., *Recorder*

Dec. 21, 1942

Gummas of the Leg with Syphilis of the Bones. Presented by DR. NATHAN PENSKY.

A. B., a man aged 39 years, born in Puerto Rico, complained of an ulcer of the right leg of six years' duration. He had never received treatment for syphilis.

Examination shows multiple punched-out ulcers on the right leg with atrophic scars and areas of hyperpigmentation. The area involved extends from the middle of the leg to the ankle and to both the inner and the outer aspect of the leg. Examination of the eyes shows that the left pupil is larger than the right, but both react to light and in accommodation. This inequality is due to a pupillary membrane and not to syphilis of the central nervous system. The right eye also shows an old healed choroiditis. Neurologic examination fails to show evidence of syphilis of the central nervous system. There was a healed scar on the penis.

The Wassermann reaction of the blood was 3 plus. Roentgenograms of the chest showed some calcification of the aorta. A roentgenogram of the leg showed the following conditions: low grade osteomyelitis involving the distal half of the shaft of the tibia, extensive osteoperiostitis of the distal two thirds of the shaft of the fibula and enormous periarticular swelling of the ankle joint.

After the patient had received two intramuscular injections of bismuth and potassium iodide by mouth, the lesions on the leg improved about 30 to 40 per cent.

DISCUSSION

DR. LOUIS CHARGIN: It is difficult, in fact almost impossible, to make a diagnosis of syphilis based on the present ulcerations. The location and the triangular outline of the lesions are not those of syphilis. The lesions lack the marginal outline one sees in syphilis. However, the healed scars, particularly higher up on the leg, are typical. They are soft, whitish, tissue-paper-like and round and show a tendency to roundness over the soft parts. The unusual feature is the fact that the other leg was also involved at one time. The fact that the patient responded so well to antisyphilitic treament would confirm the diagnosis of gumma.

DR. A. WALZER: The first impression one gets is that this is not syphilis but that the patient has had large scars of some type which broke down and produced the peculiar, irregular-shaped lesions, so that they now appear as broken-down scar tissue. The history of syphilis and results of therapy, however, support the diagnosis.

DR. NATHAN PENSKY: On admission to the clinic, the patient presented extensive involvement of the lower half of the leg. The upper portion of the leg showed several atrophic scars. The skin surrounding these scars was hyperpigmented. Below this area were extensive infiltrated areas within which were deep ulcerations and some scars. Roentgenograms of the leg were taken because in about 48 per cent of the cases gummas of the extremities are associated with involvement of bones.

In addition, the man has nonsyphilitic pupillary changes, and since about 25 per cent of patients with syphilis of bone have involvement of the central nervous system, another interesting point was brought up.

Lupus Vulgaris. Presented by DR. H. LEAVITT for DR. E. A. GAUVAIN.

Mrs. M. A., an Italian woman aged 60 years, complains of an eruption on the neck of two years' duration, with occasional mild itching. There was no history of tuberculosis in the patient or in her family.

When first seen the lesions covered the entire left side of the neck and left cheek. They consisted of salmon pink and light red soft nodules, grouped roughly in linear fashion, following the creases of the neck. None extended over the midline. The centers of the individual lesions were soft and relatively painless when pricked with a sharp pointed instrument. Infiltration and induration were minimal. The process appeared superficial. However, many thin pliable areas of cutaneous atrophy and white scars were present among the individual groups of papules. At the present time the appearance of the lesions is almost unchanged. No enlargement of cervical glands is noted.

Histologic examination of a lesion from the neck showed the epidermis to be intact for only a small area. The subcutis from the pars papillaris to the corium showed a large collection of small nodules closely packed together. The individual nodules were made up of epithelioid cells arranged in concentric fashion. Numerous atypical Langhans giant cells were observed. About the small tubercles were observed dense collections of lymphocytes. The diagnosis was lupus vulgaris.

Roentgenograms of the chest on two occasions revealed no pulmonary lesions. There were a calcified plaque in the arch of the aorta and thickening of the right costophrenic sulcus.

Two courses of contact ultraviolet irradiation with a water-cooled quartz mercury vapor arc lamp did not change the appearance of the lesions. Electrodesiccation of individual lesions produced thin, flat, white scars.

The Mantoux test with old tuberculin in a 1:100,000 dilution gave a reaction of 4 plus. In twenty-four hours there was an area of vesiculation and ulceration 1.5 cm. in diameter. A pigmented nodule 1 cm. in diameter was present three weeks after the test was made.

The Wassermann reaction of the blood was negative.

DISCUSSION

DR. D. M. DAVIDSON: It is unusual for lupus vulgaris to occur in a person of this age, but on clinical grounds the lesions, with their color and consistency, are compatible with the diagnosis of lupus vulgaris, as is the histologic structure. An interesting feature, seen infrequently in lupus vulgaris but present in this case, is the annular configuration of almost all of the lesions. The best treatment would be use of the Finsen lamp, but in its absence I suggest desiccation of the individual lesions and institution of the general tonic treatment for tuberculosis.

DR. A. WALZER: The diagnosis of lupus vulgaris is positive, and, despite the fact that the patient is 60 years of age, she undoubtedly has visceral tuberculosis, regardless of what the examination shows. As to the question of treatment, since she has a tuberculous infection elsewhere in the body and the lesions on the side of her neck do not interfere much with her general appearance, I think the best thing is to leave her alone.

DR. L. M. FRUCHTBAUM: With reference to therapy for lupus vulgaris, my colleagues and I had some experience with this type of case at the Long Island College Hospital several years ago. In 1 case, that of a woman in her early twenties, we used various destructive agents, such as desiccation and the application of chloroacetic acid, which only produced more ulceration. Any one who has had experience with therapy in these cases will certainly refrain from giving local treatment.

Dermatitis Medicamentosa (Bromides?). Presented by DR. LESSER M. FRUCHTBAUM.

E. S., a white woman aged 33 years, came to the dermatologic clinic of the Unity Hospital about Oct. 6, 1942, complaining of a rash and itch on the lower part of her leg of three months' duration. The eruption had started with a small pustule and gradually spread to a large patch, measuring 3 by 4 inches (7.5 by 10 cm.).

When she first presented herself, there was a large patch covered with crusts and scales and at the outer right margin there was a larger circinate, raised and dark red lesion with many pinpoint pustular openings at the center. However, within a week it improved, and by November 17 the lesion cleared up entirely. On November 28, a new raised dark red lesion with pustules reappeared at another site of the old erythematous patch, and a few days later the lesion improved but did not clear up entirely. On December 19, more acute lesions appeared over the old site.

The Wassermann reaction of the blood was negative.

The urinalysis revealed nothing abnormal with the exception of a trace of albumin.

The patient stated that she had been taking bromides daily for the past two years.

DISCUSSION

DR. C. T. CHIARAMONTE: The usual bromide eruption which I have seen on the lower extremities is a dusky, brownish, erythematous, granulomatous lesion. On clinical grounds alone I should be inclined to think these lesions are due to iodides rather than bromides. This can be confirmed by the findings in the urine and blood. Perhaps, in view of the history, she had the bromide eruption originally and when she was given potassium iodide the resulting effect took place. On account of the substitution the bromide may have been replaced by the iodide, and the patient later broke out with an iodide eruption. Possibly she may have an idiosyncrasy for the halogen group.

A Case for Diagnosis (Sarcoid of Boeck with Unusual Findings?). Presented by Dr. Nathan Pensky.

D. B., a white woman aged 42 years, came to the dermatologic clinic of the Israel Zion Hospital two weeks ago, complaining of a nodule on the right forearm of two years' duration. For the past ten years she had complained of a painful dorsal scoliosis.

When she was first seen, there was a firm nodular brownish pink elevated solitary lesion about the size of a nickel. After the Mantoux tests the forearm swelled to about twice its normal size and the lesion became crusted.

Roentgenograms of the chest and hands showed no abnormalities.

Mantoux tests were performed with the following results: A 1:10,000 dilution of old tuberculin gave a 4 plus reaction; a 1:1,100,000 dilution gave a 2 to 3 plus reaction, and a 1:1,000,000 dilution gave a 2 plus reaction.

Results of the histologic examination were as follows: The surface epithelium was regular, but the papillae were flattened. Occupying the entire upper layer of the corium was a broad zone of cellular infiltrate, the majority of the cells being lymphocytes. Their nuclei, however, were somewhat irregular, and the chromatin was not as uniformly and densely stained as in mature lymphocytes. They showed no great variation in size. An occasional mitosis was seen. Occasional epithelioid cells and a few small focal collections of similar cells were seen in the deeper layers, where they appeared to be grouped around distended capillaries. The diagnosis was chronic granuloma of the skin suggestive of tuberculosis.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi). Presented by Dr. Louis Chargin.

J. B., a man aged 50, born in Russia, married, a tailor by occupation, first complained of an eruption on the soles about two years ago, which gradually spread to the present extent.

Both feet are affected, the eruption being chiefly on the soles and the lateral aspects. There are scattered patches, less infiltrated, on the lower third of the legs and around the knees.

The lesions consist of flat bluish red infiltrates, small and large, some confluent. Except for some pain in the lesions on the legs, there are no subjective symptoms. The patient is otherwise in good health.

DISCUSSION

Dr. L. M. Fruchtbaum: I do not agree with this diagnosis for the following reasons: (*a*) The color of the lesions disappears on the slightest pressure; (*b*) both soles present a continuous lesion; (*c*) similar lesions present on the palms disappear on pressure, as do the lesions on the soles; (*d*) the lesions on the soles are neither raised nor infiltrated. Until a histologic examination confirms the diagnosis, I should refrain from making a diagnosis of Kaposi's sarcoma.

Dr. D. M. Davidson: This patient presents the typical picture of Kaposi's sarcoma in the erythematoangiomatous stage, and therefore some of the erythema can be expressed.

Dr. A. Walzer: There is one symptom favoring Kaposi's sarcoma. That is the verrucous lesions of the toes, which are pronounced and are frequently found in Kaposi's sarcoma.

Roentgen Dermatitis. Presented by Dr. E. A. Gauvain.

R. K., a Jewish woman aged 62, complained of itching about the vulva. She was first seen at the radiation therapy department of Kings County Hospital in 1939. At that time she stated that eleven years before she had received numerous roentgen treatments to the vulva for pruritus vulvae. After one of these treatments, a severe reaction developed with desquamation of the skin of the vulva and perineum and also of the fingers of both hands. She held the vulva open with her hands during treatments.

At present there are brawny induration, atrophy and telangiectasia of the perineum, anus and adjacent gluteal region. A similar condition exists on the dorsum of the middle and ring fingers of the right hand, and to a lesser extent on the little finger of the left hand. There are several excoriated nodules in the perineum.

A histologic study of one of these lesions has been previously reported as showing squamous cell carcinoma.

The patient has been followed since her admission to the outpatient department of Kings County Hospital. A histologic section of a crusted area showed hyperkeratosis with no malignant changes. A course of treatment with an estrogen has been administered with no improvement in symptoms. A plastic operation on the vulva, with complete removal of the involved skin and tissue, has been suggested, but the gynecologist and the plastic surgeons consulted have refused to perform it, on the grounds that there is not enough normal skin left for closure. At the present time the only treatment consists in careful periodic observation.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

FRANK C. COMBES, M.D., *Chairman*

PAUL GROSS, M.D., *Secretary*

Jan. 5, 1943

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR. LEWIS B. ROBINSON.

J. C. K., a white man aged 53 years, a pipe fitter, is presented from the Vanderbilt Clinic with a generalized eruption including the scalp, face, trunk and extremities of thirty years' duration.

The patient states that the lesions began in the center of the chest thirty years ago after an attack of "shingles" on the left side of the chest. The area was scaly and disappeared spontaneously in about a year. About twenty-five years ago similar lesions appeared on the face and scalp and also cleared spontaneously after one year. About ten or twelve years ago the arms and legs became dry and began to itch, as did also the chest. Six years ago the eruption came back on the trunk as small scaly patches that have gradually increased in size and spread to the extremities, accompanied by itching. The lesions have been present constantly since then; three or four years ago they spread to the face and scalp. The patient states that the lesions have gradually become worse during this time but that there has been no impairment of the general health.

The eruption appears the same over the entire body and is most pronounced on the back, where large palm-sized plaques desquamate freely over more or less discrete, slightly elevated, pinkish bases. These areas are confluent in many places, with clear areas between. The extremities are almost completely involved by the eruption, which appears as large, loose scales over slightly lichenified skin. The glands in both groins are enlarged to half the size of a hen's egg and are painless.

The hemoglobin content of the blood was 100 per cent; the red cells numbered 5,000,000 and the white cells 9,400. The differential count showed polymorphonuclear leukocytes 69 per cent, small lymphocytes 23 per cent, large lymphocytes 5 per cent and eosinophils 3 per cent. Urinalysis showed albumin (1 plus), an occasional white blood cell and 2 to 4 red blood cells per high power field. The Wassermann reaction of the blood was negative. Roentgen examination of the chest revealed no mediastinal thickening. The appearance of a short fissure in the middle of the pulmonary field on the right side suggested an old, healed pleurisy at this site.

Biopsy showed acute and chronic vesiculopustular dermatitis.

Previous treatment has been confined to local applications which have temporarily relieved the pruritus. The patient has never received roentgen therapy.

DISCUSSION

DR. ISADORE ROSEN: I should consider seriously a diagnosis of mycosis fungoides following a long-standing psoriasis. The lesions on the back strongly suggest the infiltrative stage of this disease.

DR. G. F. MACHACEK: In evaluating the biopsy and in view of the clinical picture, I suggest that the diagnosis of pemphigus foliaceus be considered.

DR. A. BENSON CANNON: When the patient first consulted us at the Vanderbilt Clinic, he had such a widespread dermatitis that it was difficult to get a true picture of the underlying condition. With the subsidence of the acute dermatitis, the thickened, lichenified areas were noticed on the trunk and on the back of the neck, some with a circinate outline which made one think of probable mycosis fungoides. The lesions on the scalp resembled psoriasis. We were unable to account for his unusually large inguinal glands, and we plan to remove one of them, as well as a piece of the skin, for histologic study.

DR. ADOLPH ROSTENBERG: I believe this eruption can be explained without the assumption, unconfirmed by biopsy, that it is mycosis fungoides. It is a well known fact that a long-standing psoriasis may terminate in dermatitis exfoliativa.

DR. MAURICE J. COSTELLO: The patient states that he received intravenous injections of an amber-colored fluid twice a week for six months, which he believes made the eruption worse. He may have received some type of arsenic.

Neurofibromatosis of the Palms and Wrists. Keloids. Presented by DR. BEATRICE M. KESTEN.

C. D., a woman aged 35 years, is presented from Vanderbilt Clinic with neurofibromas along the tendon sheaths of all the fingers, particularly at the joints, in the middle of the palms and on the wrists.

Just before her first pregnancy the patient noted hard lumps on the fingers, which increased to about 1 inch (2.5 cm.) in diameter. They were not painful until five or six years ago. Some new lesions have appeared since that time. Any direct stimulus, such as cold, contact or change in temperature, causes pain which may radiate as far as the elbows. The patient has been practically invalided. In March 1942, after complete neurologic consultation and study, neurofibromas were excised from three fingers of the right hand. The lesions were immediately under the skin, and nerve fibers were seen coursing along the surface of these fusiform masses. The majority of the nerve fibers went directly through the masses, which made it necessary to destroy a large percentage of the sensory nerve fibers. After excision of these neurofibromas, the skin healed rapidly, and within a few weeks keloids were forming at the six sites of incision, along the medial and lateral surfaces of the three fingers.

Examination showed symmetric, skin-colored tumors on both palms, all less than 2 cm. in diameter, some following the tendon sheaths and extending about 3 cm. The average number is about six on the fingers and nine on the thumbs. The masses are firm, adherent to both skin and underlying tissue and definitely painful. The neurologic status was normal except for pain on pressure over the lesions; the mental status was normal.

A blood count, a urinalysis, an examination of the spinal fluid and a roentgenogram of the cervical portion of the spine all indicated normal conditions, and the Wassermann reaction of the blood was negative.

Roentgenograms of the hands showed trabecular coarsening of the proximal phalanx of the second finger of the right hand not unlike that sometimes observed in patients with sarcoid.

Microscopic examination of neurofibromas removed from the fingers showed a number of fragments of dense connective tissue and some loose-meshed fibrous tissue, through which ran bundles of elongated cells in parallel rows embedded in dense connective tissue. These bundles frequently intertwined with bundles running at angles to them. The elongated cells of these bundles were poorly outlined and had long, slender, deep-staining nuclei. The latter at times were in palisade formations. Between the bundles, the tissue was loose meshed and poorly cellular, some of the cells being stellate. Among these were some mast cells. Occasionally amorphous pink material was seen in these zones, and in such material lipid-laden phagocytes were encountered. Occasionally small accumulations of bluish, stringy material were found in the loose-meshed zones surrounding one or more cell bundles. A number of nerve bundles were found passing through these fibrous masses, and when stained for myelin they were found to be partly demyelinated. With phosphotungstic acid stain there was found to be a good deal of collagen in the cellular bundles.

Since the removal of the neurofibromas, the patient has had no pain in the involved lesions and has acquired no new ones. However, keloids have developed, and the patient has no sensation in these fingers. In addition to the neurofibromatosis, the patient has multiple keloids on the chest and arms at the site of a recent incision.

DISCUSSION

DR. CHARLES WOLF: There are interesting and unique features in this case. First, the localization is unusual for neurofibroma; secondly, there is the extreme pain in the lesions still remaining. However, we cannot gainsay the pathologic report. I suggest that in view of the exquisite pain in the remaining lesions the disease may be multiple neuroma.

DR. A. BENSON CANNON: I also thought that this was an unusual case. I was told that the patient had von Recklinghausen's disease, whereas the lesions were those of neurofibroma. There was no evidence of the former disease. The patient was studied at the Neurological Institute. Histologic examinations of the tumors were made, and there was little doubt as to the diagnosis of neurofibroma.

DR. FRED WISE: I believe the case is presented not as one of von Recklinghausen's disease but as one of neurofibroma. The disease is really an isolated variety of neurofibroma, in contradistinction to generalized neurofibromatosis. I agree with Dr. Wolf that the localization is unusual.

DR. FRANK C. COMBES: It is a very unusual case. I have encountered 1 other, that of a soldier with a lesion on one hand, in which a diagnosis of neurofibroma was made.

DR. BEATRICE M. KESTEN: I do not know of any histologic difference between neurofibromatosis and von Recklinghausen's disease. This case was presented as an instance of neurofibromatosis, a diagnosis made largely from histologic study. I should be grateful if some one would tell us the histologic differences between the two diseases.

Syphilitic Gumma of the Pharynx. Presented by DR. A. BENSON CANNON.

R. P., a white girl aged 6 years, is presented from the Vanderbilt Clinic with a lesion of the pharynx of four months' duration.

The patient had pertussis during early summer, for which she received four inoculations, and on August 4 she was vaccinated, without severe reaction. About four months ago the mother noticed that the child had a fetid breath and on examination of the mouth saw an ulcerating area on the back part of the pharynx. The patient did not complain that her throat was sore. A local physician was called, who made smears, which did not reveal diphtheria organisms or Vincent's organisms but did yield hemolytic streptococci. A powder spray of one of the sulfonamide compounds was tried, without success.

Neither the patient nor her parents have received antisyphilitic treatment. The mother states that the Wassermann reaction of her own blood was negative while she was pregnant. There are no other children.

Examination shows no evidence of congenital syphilis. The eyes, teeth, nose, facies and joints are normal. On the posterior wall of the pharynx and involving the posterior tonsillar pillars is a sloughing, granular area that appears covered with a grayish membrane and extends up into the nasopharynx and down to the epiglottis but does not involve the vocal cords. There are no lesions in the mouth, in the anal and genital regions or on the skin.

The Wassermann reaction of the blood of the patient and both parents was 4 plus. The patient's spinal fluid gave a negative Wassermann reaction. A Mantoux test with a dilution of 1:1,000 was negative. Cultures of material from the pharynx did not contain diphtheria organisms but yielded hemolytic streptococci. Roentgen examination of the bones of the skull and extremities showed no chronic osteitis.

A blood count revealed a hemoglobin content of 100 per cent, 4,800,000 red cells and 10,500 white cells, of which polymorphonuclear leukocytes comprised 60 per cent, lymphocytes 36 per cent and monocytes 4 per cent. Urinalysis gave values within normal limits.

Histologic examination disclosed granulations covered by a purulent crust with bacterial clumps. Within the mass of granulomatous proliferation were diffusely scattered spindle-shaped cells. Some were palisaded about areas of necrosis. Several giant cells were present. No typical tubercles were evident. The lesion was morphologically consistent with a diagnosis of gumma.

The lesion has been unaffected by the administration of sufficient sulfadiazine orally to maintain a blood level of 4 to 6 mg. per hundred cubic centimeters for eighteen days.

NOTE.—Since presentation two months ago, the patient has received weekly intramuscular injections of bismuth subsalicylate in oil totaling 8 cc. (0.8 Gm. of the bismuth compound). No iodides or any other medication has been given. The ulcerating lesion is now healed.

DISCUSSION

DR. JEROME K. FISHER: It is rather unusual for a child of 6 years to have a gumma. The mother states that to her knowledge there is no history of syphilis in the family. I was not able to question the father.

Localized Myxedema. Presented by DR. LOUIS TULIPAN.

E. W., a woman aged 41 years, a patient at the New York University dermatologic clinic, noticed a tremor of the hands and bulging of the eyes in 1940. In May of that year a thyroidectomy was performed in Denmark. One year later, she noticed small lumps on both legs anteriorly, and these were followed by several more on the surrounding skin. There were no symptoms.

The patient now presents thickened, elongated plaques 5 by 3 inches (12.7 by 7.5 cm.) in size over the tibias. These are pale red, infiltrated and edematous, with an irregular surface and gaping follicles which do not pit on pressure.

The basal metabolic rate was +9 per cent. The pulse rate was 80. Examination of blood and urine gave normal results.

Histologic examination of one of the lesions showed an area of frayed and ruptured collagen in the upper portion of the corium which was fairly well defined. This area showed tinctorial degeneration of collagen to several selective stains but did not stain blue with hematoxylin. The reaction was negative for amyloid. There were several perivascular cuffs of infiltration deeper in the corium but no other pathologic signs. The epidermis was normal. There was

a slight reaction for mucin in the area of degeneration. In the area of degenerated collagen there were numerous vacuoles giving the appearance that some substance had been dissolved out. This is a case of degeneration of collagen of unknown origin.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: This is a classic example of localized myxedema. Lesions of this sort appear in patients with hyperthyroidism who have had a thyroidectomy. The patients apparently have periods of hypothyroidism, which probably account for the development of localized myxedema on the legs.

DR. LOUIS TULIPAN: The only other fact to which I should like to draw attention is that histologic examination did not show the excessive amount of mucin which is supposed to be characteristic. In such cases there is no response to administration of thyroid, as has been proved in this instance. The patient has been receiving thyroid for some time.

DR. G. F. MACHACEK: I have examined a number of patients with these symptoms and, while the morphologic changes are more or less similar, mucin is a variable factor.

Prickle Cell Epithelioma. Presented by DR. FRANK C. COMBES.

S. U., a man aged 62 years, is presented from Bellevue Hospital with a lesion on the right forearm of four and a half months' duration.

The patient claims that he was bitten by a mosquito and scratched the site. Later he applied the leaf of a plant (dog tongue) and a variety of ointments.

There is an oval lesion on the external aspect of the right forearm measuring 1½ by 1 inch (3.4 by 2.5 cm.). It is broken down, brownish and necrotic in the center and exhibits some undermining toward the margin, which is raised, rounded, smooth and dusky red. There is a purulent discharge from the undermined area. The border is firm, fleshy and painless. There is no surrounding inflammatory reaction, and the lesion is not fixed to the underlying structures. No axillary or epitrochlear adenopathy is present.

Smears show numerous pus cells with streptococci and staphylococci. Culture on Sabouraud's medium produced an abundant growth of staphylococci but no fungi. Smears from the tissue did not show acid-fast bacilli.

Urinalysis gave normal results, and the Wassermann and Kahn reactions of the blood were negative.

Biopsy revealed prickle cell epithelioma.

DISCUSSION

DR. A. BENSON CANNON: In its configuration, its fungating character and the softness of the growth this lesion in no way resembles an epithelioma. I should advocate its total surgical removal and histologic study.

DR. MAURICE J. COSTELLO: The patient has been rather thoroughly studied. Blastomycetes and ray fungi were not found on microscopic examination. I believe two pathologists examined the biopsy specimen. One thought the lesion was a verruca, and the other believed it to be a prickle cell epithelioma.

DR. FRANK C. COMBES: I agree with Dr. Cannon about the unusual appearance of the lesion, which does not have the characteristics of prickle cell epithelioma of the extremities. When we first saw the patient, the lesion was exuding thick pus and the border was spongy, which led me to make a clinical diagnosis of possible sporotrichosis of the epidermal type on first examination. Then we obtained a history which was more convincing. There was no preexisting lesion here and no keratosis. The patient gave a history of having a mosquito bite which he scratched and to which he then applied the leaf of a plant. This happened in New Jersey, where we recently had a number of cases of sporotrichosis. Cultures have produced a growth of Sporotrichum, and the biopsy definitely indicates prickle cell epithelioma. The original pathologic report, as Dr. Costello said, was that the lesion was verruca, and in parts it looks as if it were, but in other parts there is definitely carcinomatous degeneration.

Leiomyoma. Presented by DR. J. LOWRY MILLER.

T. B., a man aged 45 years, is presented from Vanderbilt Clinic with lesions of the face, trunk, left arm and left calf of sixteen years' duration. He was first seen in the Vanderbilt Clinic in 1931, with pea-sized bluish red firm nodules located on both sides of the face, on the left leg and on the trunk. These had been present for five years. They were not tender to touch but ached in cold weather and bled freely when cut. Two lesions were removed, one by electrodesiccation and one by surgical excision. A number of smaller, softer lesions were noted at the time.

Eleven years later, in November 1942, the patient returned complaining of similar nodules on the face, trunk, left arm and left leg. Several of these were exquisitely painful when pressed between the fingers. Pressure on other nodules elicited no particular pain. A painful and a nonpainful nodule were removed for histologic study. There was no evidence of recurrence of lesions in the scars made by removal of nodules eleven years previously.

The Wassermann reaction of the blood in 1942 was negative. After a biopsy in 1931 the lesion was reported as leiomyoma. Biopsy of a painful lesion in 1942 disclosed a lobulated infiltration within the cutis. The cells were spindle shaped, with the typical appearance of smooth muscle cells. Their arrangement was also typical of smooth muscle bundles. This was borne out by staining with both Masson's trichrome and Van Gieson's stain. The tumor mass was separated from the epidermis by a narrow zone of cutis and in some places seemed to be almost in contact with it. The epidermis showed long penetrating rete pegs except where the tumor was close to the epidermis. Hyperkeratosis and parakeratosis were present. A chronic inflammatory reaction was noted. The diagnosis was leiomyoma.

Section of a painless lesion from the chest in 1942 showed a nodule of spindle-shaped cells which in appearance and arrangement were typical of a smooth muscle cell tumor. This was borne out by Masson's trichrome and Van Gieson's stain. The tumor was separated from the epidermis by a band of corium. The diagnosis was leiomyoma.

Tuberculosis of Cutis and Hypoderm Associated with Genitourinary Tuberculosis and Chronic Pulmonary Tuberculosis. Presented by DR. F. PHILIP LOWENFISH.

W. T., a white man aged 55 years, is presented from the Vanderbilt Clinic complaining of a lesion on the right elbow of fourteen months' duration. When he was first seen, on Jan. 16, 1942, there was an erythematous infiltrated plaquelike lesion on the extensor surface of the right elbow. It was covered with whitish scales suggestive of psoriasis, but when they were removed no bleeding points were present and discrete small scaly red papules resembling lichen scrofulosus were seen. A walnut-sized firm lump simulating a juxta-articular node was present near the medial condyle. It was freely movable and nontender. In view of the patient's past history, a biopsy was made of a specimen from the skin; the lump was completely excised and sectioned, and guinea pigs were inoculated with materials from both specimens.

The patient has been studied in the urologic department of the Presbyterian Hospital and in the Vanderbilt Clinic at various times during the last ten years. The diagnoses made at the Presbyterian Hospital were: (1) bilateral renal and vesical tuberculosis; (2) tuberculosis of seminal vesicles; (3) tuberculous epididymitis (right); (4) postoperative absence of left testis and epididymis, and (5) moderately advanced chronic pulmonary tuberculosis.

Tests with old tuberculin gave negative reactions with dilutions of 1:1,000,000, 1:100,000 and 1:10,000 and a positive reaction with a dilution of 1:1,000. Red and white blood cell counts were normal; the Wassermann and Kline reactions were negative, and examination of the sputum did not reveal tubercle bacilli. The urine constantly showed albumin (2 plus) and an occasional red blood cell. About three months prior to the onset of the cutaneous eruption, twenty-four hour specimens of urine contained acid-fast bacilli.

Biopsy revealed tuberculosis of the cutis and hypoderm, clinically lichenoid. Acid-fast bacilli were found in the caseating lesion of the hypoderm.

Materials from the cutaneous lesion and from the lesion of the hypoderm did not produce tuberculosis when inoculated into guinea pigs. The lesions were grossly positive for tuberculosis and microscopically positive for tubercles and acid-fast bacilli.

Roentgen examination of the elbow in the anterior-posterior and lateral projections showed no osseous abnormality.

Treatment has consisted of ultraviolet irradiation once weekly to the chest, back and right elbow and administration of 1 tablespoon of cod liver oil three times a day. The lesion has improved and is fainter. The patient feels much better and has gained weight.

Book Reviews

Diseases of the Skin. By Oliver S. Ormsby, M.D., Rush Professor of Dermatology, University. of Illinois, and Hamilton Montgomery, M.D., MS., Associate Professor of Dermatology and Syphilology, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minn. Sixth edition. Price $14.00. Pp. 1,360, with 654 figures containing 723 illustrations and 6 colored plates. Philadelphia: Lea & Febiger, Publishers, 1943.

Every new edition of Ormsby's classic textbook is welcomed by dermatologists. It is interesting to note that the new junior author of the sixth edition is the son of Dr. Frank Montgomery, who wrote a previous text as senior, with Dr. Ormsby as junior, author. The combined experience of the two authors in both clinical and pathologic aspects of dermatology is ideal for the production of a textbook that reflects the greatest credit to them and adds prestige to American dermatology.

The present edition has been thoroughly revised. One new chapter, unfortunately too short, on the chemistry of the skin and one new class of diseases (metabolic) have been added. The book contains descriptions of twenty-two diseases not included in previous editions. The material on many other diseases has been almost completely rewritten, notably the chapters on neoplasms and lymphoblastomas, on pigmentary disturbances and on diseases of metabolism, especially the xanthomas and the scleroderma and dermatomyositis group.

The histologic sections have been greatly enlarged and revised and, to save space, appear in fine print. All the histologic and mycologic sections have been revised by Dr. Clark Finnerud with the cooperation of the junior author, whose special knowledge of histopathology of the skin is well recognized.

A feature of the book, which is printed on glazed paper throughout, is the excellent selection of a large number of unusually fine illustrations. These include histologic and mycologic reproductions. A few colored illustrations are included, though, considering the cost, the reviewer considers them of doubtful value. Many authors are cited in the text, and an adequate bibliography is provided.

It is unfortunate that this splendid textbook should be marred by the failure, in many instances, to follow the "Standard Nomenclature of Disease," and by the presence of numerous mistakes in Latin terminations of names of diseases. It is also confusing that different titles are given to illustrations of the same disease. It is hoped that these errors will be corrected in the next edition, for which there will surely be a demand.

The book is highly recommended to students and practitioners of dermatology. It should be an essential addition to the library of every dermatologist. The work of the publishers is up to their usual high standard.